VOLUME 59 NUMBER 3

ARCHIVES OF SURGERY

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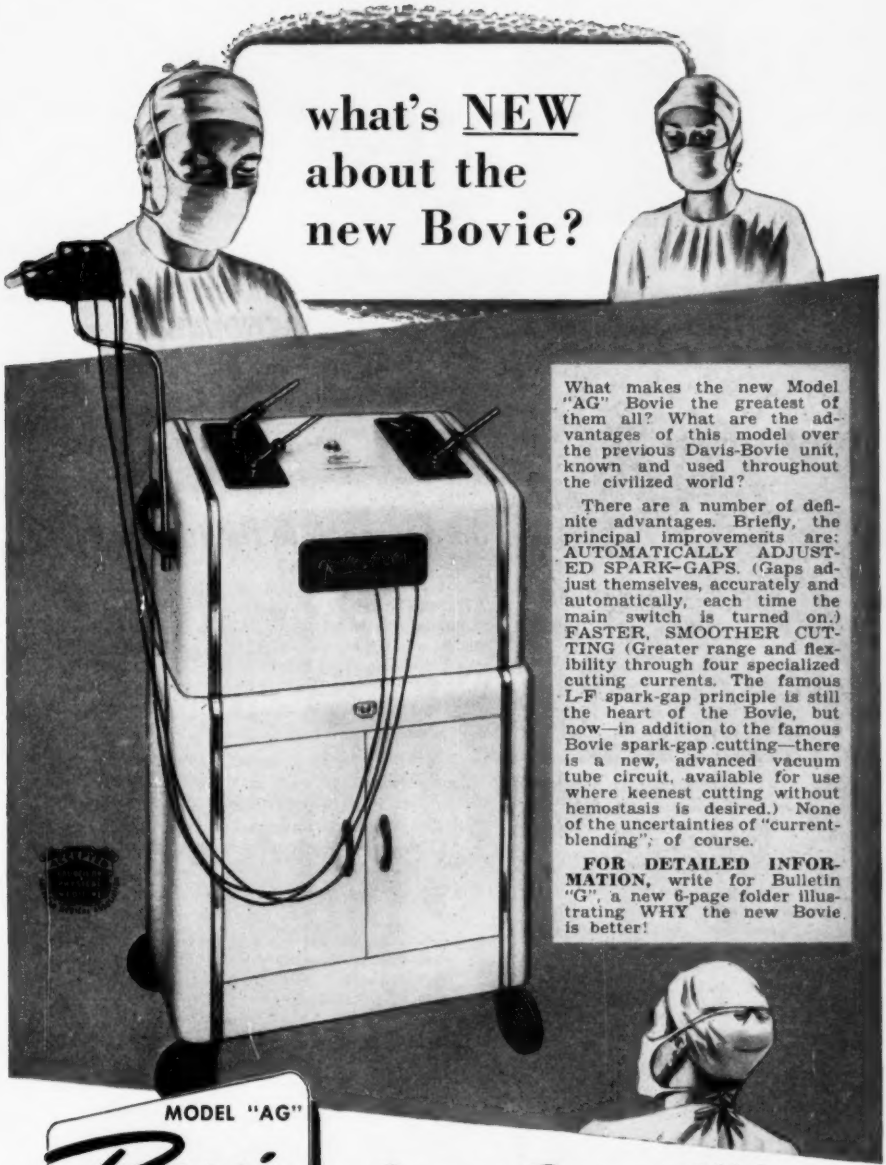
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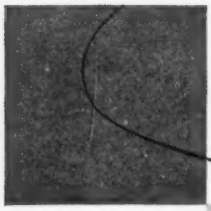

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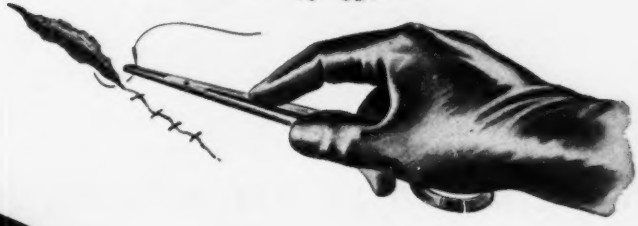

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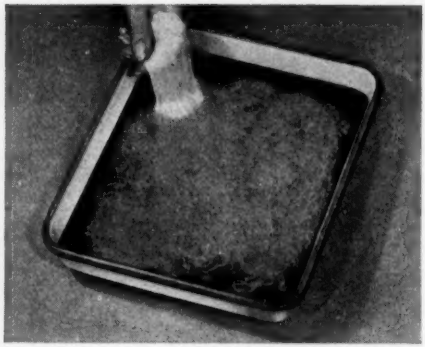

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ARCHIVES OF SURGERY

VOLUME 59 SEPTEMBER 1949 NUMBER 3

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ORIGINS OF THE NATIONAL AND REGIONAL SURGICAL SOCIETIES

Presidential Address

HENRY K. RANSOM, M.D.
ANN ARBOR, MICH.

THE MIDDLE of the nineteenth century was a notable epoch in the chronicles of American medicine. The demonstration of ether anesthesia to a medical group in 1846 was followed by the rapid development of the medical sciences, particularly cellular pathology, bacteriology, organic chemistry and experimental physiology. Through the application of the knowledge derived from the basic sciences to clinical practice, medicine gradually emerged from the age of theories and systems and assumed its position as one of the major disciplines of biology. Furthermore, attempts to regulate certain aspects of medical practice were introduced during this period. In 1847, the American Medical Association was founded, chiefly for the purpose of improving the state of medical education but also to combat the evil of college faculties' both teaching and licensing medical students. In 1860, the scientific sessions of this body were divided into four sections, one of which was surgery. For some twenty years this surgical section of the American Medical Association was the only national forum at which physicians from all parts of the country interested in surgery could convene, exchange views and compare experiences. Surgery at that time was almost static, its scope was limited, there were no surgical specialists and all surgeons were general practitioners. The attendance at these yearly meetings of the surgical section was large, since it was purely voluntary, and no attempts were made to limit participation to those having special qualifications in surgery.

It was not until Lister succeeded in transferring the discoveries of Pasteur to the management of surgical wounds that elective operations within the abdominal cavity, the thoracic cage, the cranial chamber and the joints were made possible. With the field of surgical endeavor thus enlarged, the number and variety of surgical operations in all hospitals increased at a rapid rate and ingenious surgeons were quick to devise new procedures and when necessary to discard or modify the older

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

ones. Knowledge of surgery thus accumulated rapidly, although the opportunities for this type of surgical education were not available equally to all. Those most fortunate in this respect were the chiefs of the surgical clinics in the large hospitals, then situated for the most part along the eastern seaboard. These men, having the control of clinical material, were able to amass a vast amount of information and by thoughtful study to formulate well considered opinions and to chart new fields for exploration. Certain of these physicians in the vanguard of surgical progress foresaw the advantages to be gained through the establishment of special national organizations comprising a restricted number of physicians from different parts of the country having a common purpose and working under similar conditions.

Such a man was James Read Chadwick (1844-1905), of Boston, best known to succeeding generations of medical students and physicians through the eponym, Chadwick's sign of pregnancy. Chadwick, surgeon, bibliophile, collecter, teacher and humanitarian, after graduation from the Harvard University Medical School in 1871, spent two years abroad studying in Berlin, Vienna, Paris and London in accordance with the custom of the day. Early in his career, he evinced special interest in the then new specialty, gynecology, and on entering practice became gynecologic surgeon to the Boston City Hospital. It was he who, while still a young man, conceived the idea of a small national association to be composed of representative men whose reputations in the field of obstetrics and gynecology were already established. He believed the centennial year to be a propitious time for the founding of such a society, and, accordingly, with the assistance of J. Tabor Johnson, Paul Munde and E. R. Peaslee, he formulated a plan for an American Gynecological Society. An organizational meeting was held in New York, June 3, 1876. At this time it was agreed that the society should have a restricted membership and that the qualifications of candidates for admission should be high. It was believed that thereby membership "would be coveted and sought after and the discussions would be more profitable." The first annual meeting was held in New York, Sept. 13, 14 and 15, 1876, with Fordyce Barker the first president and Chadwick the first secretary, an office which he held for seven years. By virtue of his ability, commanding personality and tact, Chadwick did much to secure able men as a nucleus for the organization and to maintain the high ideals set by the founders. At first, membership was limited to sixty, this number later being increased to one hundred. The original constitution gave as the object of the society, "the promotion of all that relates to the diseases of women and to obstetrics," while subsequently the phrase "and to abdominal surgery" was added. In the beginning, the council voted to publish yearly

transactions of the meetings and with the assistance of John Shaw Billings, then in charge of the National Medical Library in Washington, to append to each volume a complete bibliography of all of the literature pertaining to obstetrics and gynecology of that year. In the early years of the society, candidates for admission were required to present to the executive council a paper embodying original work of either a clinical or an experimental nature. The papers of those candidates elected to membership were published in a special section of the following volume of the transactions.

The motto selected for the society was the following quotation from Goethe:

Wie das Gestirn
Ohne Hast
Aber ohne Rast
Drehe sich jeder
Um die eigene Last

Without question, the most eminent surgeon of his time was Samuel David Gross (1805-1884), of Philadelphia. A peerless surgeon endowed with a sterling character, a benevolent disposition and dignified mien, and possessing a profound knowledge of his subject, he was one of the most inspiring and influential teachers of his day. Born of German parents in Easton, Pa., Gross received both his preliminary and his professional education in America. After graduation from the Jefferson Medical College of Philadelphia in 1828, he held teaching positions in the medical schools of Ohio, Cincinnati and Louisville, finally returning to his alma mater in 1856 as professor of surgery. He was a scholarly and prolific writer in the fields of both clinical and experimental surgery and played an important role in the development of surgical pathology. His "Elements of Pathological Anatomy" in two volumes, published in 1839, was one of the classics of his time.

With his customary broad vision, Gross believed that among the sixty thousand physicians in the United States, there was a group of surgeons whose professional skill and ability as teachers and writers was such that their organization into a national association would be of distinct advantage and that this would serve "to embody in one harmonius whole, the surgical talent and wisdom of this great country." Accordingly, with the aid of his close friends, Moses Gunn, William T. Briggs and William W. Dawson, his plan for an American Surgical Association was brought before the members attending the surgical section of the American Medical Association at its meeting in Atlanta, Ga., in May 1879. The idea of such an annual consultation of surgeons met with favorable response, and, accordingly, the principal surgeons of the United States were invited to attend an executive session the next year, again at the time of the meeting of the American Medical Association.

At this time Gross was elected the first president, which office he held until 1884, when he was succeeded by Edward M. Moore. He has the unique distinction of being the only member ever to serve as president for more than one year. A final preliminary meeting was held in May 1881, followed by the first scientific session at Coney Island four months later. The first volume of the transactions was published in 1883 and contained the reports of the first three regular meetings. According to the original constitution, the number of members was limited to one hundred. In 1883 an amendment raising this to one hundred and fifty failed to pass because it was feared the association would become unwieldy. Later, however, this amendment was adopted. No further change occurred until 1934, when the limit was raised to one hundred and seventy-five, and only very recently has this been increased to two hundred and fifty. In accordance with the original custom, the annual meetings continue for three days and are held in the late spring, a time originally chosen in order to follow the termination of the school year. The official seal of the association bears the profile of Samuel Gross.

Prior to the turn of the century, there were few surgeons who restricted their work to urology, although important contributions in this field had been made by such men as Bigelow, Arthur Tracy Cabot, Van Buren, Fuller, Gouley and others. Genitourinary surgery at that time was concerned chiefly with disorders of the male urethra and prostate and occasionally with bladder stone, and it was often combined with syphilology. Edward Lawrence Keyes (1842-1924), one of the leading genitourinary surgeons of his day, did much to clarify the status of urology and to elevate it to the dignity of an independent surgical specialty. Much of his influence was exerted through a textbook published in 1874 and entitled, "A Practical Treatise on the Surgical Diseases of the Genito-Urinary Organs Including Syphilis," of which he was co-author with Van Buren. Educated at Yale and the New York University Medical College, Keyes then spent a year in Paris studying dermatology. On his return to New York, he was appointed professor of dermatology in the Woman's Medical College of the New York Infirmary for Women and Children. He later became professor of dermatology, syphilology and genito-urinary surgery at the Bellevue Hospital Medical College, and at the Bellevue Hospital he unofficially established what was probably the first urologic ward in this country.

In view of his admirable achievements as a teacher, clinician and investigator, it was logical that he should have been the founder of the American Association of Genito-Urinary Surgeons. On Oct. 16, 1886, at the invitation of Keyes, a meeting was held at 1 Park Avenue for the purpose of organizing a society to be devoted to the study of genito-urinary and venereal diseases. At this meeting, at which there were

eleven guests, mostly from Boston and New York, the necessity for and advantages of such an association composed of surgeons from the several parts of the country were discussed. It was agreed that the study of syphilis should be included in the proposed work of the society. Keyes was elected the first president. The first annual meeting was held at Lakewood, N. J., May 17 and 18, 1887, and the papers presented at this session were subsequently published in the *Journal of Cutaneous and Genito-Urinary Diseases.* From the first, urologic subjects dominated the programs and during the ensuing twenty-five years papers pertaining to venereal disease and syphilis gradually diminished in number and the interests of the group finally became concentrated on problems in urologic surgery. It was not until 1907 that the publication of yearly transactions of the association was begun. The number of members according to the original constitution was limited to fifty, although in 1905 this was increased to sixty.

The idea of an American Orthopedic Association and plans for such were evolved independently by Newton M. Shaffer (1846-1928) and Virgil P. Gibney (1847-1927), of New York. Both of the founders were pioneers in the field of orthopedic surgery, and both had long and distinguished records of service at the Hospital for the Ruptured and Crippled. The plans of these two men were consolidated at a meeting at the home of Shaffer on Jan. 29, 1887, when a group of men interested in the subject was invited to consider formally the formation of such an organization. It was agreed that there was need for this type of an association, first, to bring together American orthopedic surgeons and, second, to secure better recognition in Europe of American orthopedic surgery. Plans for the organization were drawn up, and the first annual meeting was held at the Academy of Medicine in New York, June 15 and 16, 1887, when Shaffer was honored by being made the first president. The aim of the organization as given in the constitution was the advancement of orthopedic science and art. Members were to be graduates in medicine, in good professional standing and especially interested in orthopedic surgery. Candidates for admission were to have been in the practice of medicine for at least three years and should have given evidence of satisfactory scientific attainment. There were thirty-five names on the original roster of members. In 1890, a proposed amendment limiting the number of members to fifty was voted on and lost. At the present time, the number is not to exceed two hundred. For fifteen years the transactions were published annually. Beginning in 1903 this was discontinued, and papers presented at the meetings were published in the new *American Journal of Orthopedic Surgery,* a periodical published by the Association, which replaced the transactions.

It is of interest that in 1888 a second national society in the field of obstetrics and gynecology was formed. This organizaton came into

existence largely because of the efforts of Albert Vanderveer (1841-1929), then professor of clinical, didactic and abdominal surgery in the Albany Medical College, and of W. W. Potter (1838-1911), of Buffalo. The reasons for the formation of this society were set forth by Adam H. Wright in his presidential address in 1891, when he recalled that in 1886 the Congress of American Physicians and Surgeons had been organized and was designed to serve as a federation embracing all the organized special societies. Its by-laws stated that the congress should be composed of national associations for the promotion of medical and allied sciences and that it should hold its sessions triennially in the city of Washington, D. C. Obstetrics and gynecology was the only important specialty not represented at that time. Friends of the congress believed that if a society in this field were properly organized it would obtain admittance to the congress. Accordingly, an invitation was issued to certain men representative of abdominal surgery, obstetrics and gynecology in various parts of the United States to assemble and consider the wisdom of effecting such an organization. Fifteen men gathered at "The Niagara" in Buffalo, on April 19, 1888. Plans for the formation of the American Association of Obstetricians and Gynecologists were completed, and the first annual meeting was held the following fall. While this organization was not subsequently admitted to the congress, as had been hoped and planned, nevertheless a flourishing society came into existence and it has continued through the years to have contributed greatly to the expansion of the general fund of knowledge in this special domain. The membership was originally restricted to one hundred, whereas at the present time it is set at one hundred and fifty. From the beginning, an annual transactions has been published, and since 1920 the *American Journal of Obstetrics and Gynecology* has been the official organ of both this association and the American Gynecological Society. In 1920 the name of the society was changed to the one used at present, the American Association of Obstetricians, Gynecologists and Abdominal Surgeons.

With the increase in the scope and importance of surgery following the advent of the aseptic method, the educational value and constructive work of the national surgical societies were convincingly demonstrated. However, because of their restricted membership and the fact that they were dominated by the large medical centers of the East, many able men in other sections of the country, particularly in the South and the West, were denied the stimulation, the social advantages and educational value of such meetings. Moreover, travel at that period was time consuming and difficult. It naturally followed that the demands and needs of these groups were met by the further extension of organized surgical societies in the form of sectional or regional organizations having a pattern similar

to that of the older national groups. Two of the earliest and best examples of this trend are to be found in the origins of the Southern Surgical Association and of the Western Surgical Association.

The Southern Surgical Association came into existence through the earnest and untiring efforts of William E. B. Davis (1863-1903), of Birmingham, Ala. Davis, early in his medical career, chose abdominal surgery and gynecology as his chief field of interest, and he held the chair of gynecology and abdominal surgery in the Birmingham Medical College, of which he was a founder. In order to provide the surgeons of his locality with the advantages to be derived from participation in surgical meetings of a high order, in 1886 he became the organizer of the Surgical and Gynecological Society of Alabama, despite considerable opposition by many of his colleagues. This organization had a brief existence, as its first and only meeting was held in October 1887. However, from it stemmed the Southern Surgical and Gynecological Association, a more comprehensive society, plans for which were considered at this 1887 meeting. W. D. Haggard Sr., the first president, in his annual address, pointed out that the Southern Association was not intended to remain purely sectional in character but that prominent surgeons from other parts of the country were to be invited to meet with the surgeons of the South for the exchange of ideas and discussion of experiences and to encourage the undertaking of and reporting of original work, especially by the younger men. The region served included the eleven original Southern states and also Kentucky, Maryland, Missouri and the District of Columbia. By tradition, all officers have been residents of these states, and with but two exceptions no meetings have been held outside of this Southern territory. Although originally there was no constitutional limit to the number of members, it was the intention of the founders to restrict the membership to one hundred. By 1891, however, because of the rapid growth and popularity of the association, it became necessary officially to limit it to one hundred and fifty, and in 1902 this number was advanced to two hundred, where it has remained. In 1917 the name of the organization was changed to the Southern Surgical Association. Nevertheless, papers in the field of gynecology have continued to appear on the programs and this specialty is represented by an appreciable number of members. A permanent record of the meetings has been preserved in the annual transactions. A miniature portrait of Ephraim McDowell of ovariotomy fame constitutes the official seal of the organization.

In the early nineties of the last century, the western part of the United States was relatively undeveloped and methods of communication and transportation were primitive. For these reasons a group of men, most of them obstetricians and gynecologists, concurred in the idea

that a society composed of surgeons residing in the Western states which would meet at some point accessible to most of them would be desirable. Credit for developing this idea into a realization goes to Milo B. Ward (1848-1901), one of the prominent gynecologists of Topeka, Kan., and a pupil of Joseph Price, of Philadelphia. At Ward's invitation the group convened in Topeka on Oct. 5, 1891, made preliminary plans and adopted the name, The Western Association of Obstetricians and Gynecologists, presumably because the greater part of the surgery of that period was of this type. In December 1891, the first regular meeting was held in Topeka, when the details of organization were completed and Ward was chosen the first president. According to the original plans, the members were to be men who were giving special attention to the practice of obstetrics and gynecology and who resided in the Missouri River cities of Iowa and Missouri and the states of Kansas, Nebraska, Colorado, New Mexico, Indian Territory and Oklahoma. Since then the territory covered by the Association has been enlarged so that all the Western states are now included. The earlier programs were published somewhat sporadically, usually in the *Journal of the Kansas Medical Society*. Beginning in 1897, the record of this entire meeting was published in book form as a transactions, and that policy has been continued to the present time. Gradually the topics of papers presented included more and more subjects of a general surgical nature, and in 1895 the title was changed to the Western Surgical and Gynecological Association. This persisted until 1909, when it became The Western Surgical Association. Originally, membership was limited to one hundred. In 1903 this was increased to one hundred and fifty, in 1929 to one hundred and seventy-five and in 1948 to two hundred.

Shortly after the turn of the century, some of the more ambitious and enthusiastic younger surgeons became dissatisfied with the existing policies of medical societies and the conduct of medical meetings. They resented the ultraconservative, exclusive and inflexible policies of the older surgical societies with regard to the admission of younger men to membership and also the formality and pedantic didacticism which characterized some of the programs. Since the prevailing order, strengthened by long tradition, could not easily be altered, a small number of this rebellious younger group, all holding university positions, decided to form a new society, the activities of which would be conducted along entirely different lines. Cushing related that possibly the idea of a clinical surgical society was first discussed by W. J. Mayo, A. J. Ochsner and himself in 1900 while they were attending the Twelfth International Medical Congress in Paris. However, it remained for George Crile

(1864-1943) to take the initiative in the actual formation of such a new society, and, accordingly, he and James Mumford invited a small group of their colleagues to meet in New York for the purpose of organization. On July 11, 1903, at the Murray Hill Hotel, the Society of Clinical Surgery was officially founded. The original members included George Crile, James G. Mumford, John C. Munro, Charles H. Frazier, George E. Brewer and Harvey Cushing. Most of these men were then in their thirties, and the age for retirement from active membership was set at 55. Crile formulated a plan for the conduct of the meetings which comprised his seven commandments. In summary these were: 1. No formal papers should be read. 2. Nothing presented at a meeting was to be published. 3. The meetings were to be in the form of demonstrations and to be held at the hospital where the surgeon entertaining the society worked. 4. Business sessions and entertainment were to be kept to a minimum. The aim of the society, according to Crile, was "a minimum of proceedings and a maximum of ideas—a 'show-me' society for mutual benefit." The first regular meeting was held in Baltimore and Philadelphia, Nov. 13 and 14, 1903, with J. M. T. Finney the first president. Originally it was planned to have two two day meetings a year, each meeting to include operative clinics in two neighboring cities, such as Baltimore and Philadelphia, New York and Boston, Cleveland and Buffalo and Chicago and Rochester, Minn. Later it was deemed advisable to hold the two day program in one city. Having made a complete circuit of the United States twice, the first meeting abroad was held in 1910, the visit including the medical centers of the British Isles, where in Great Britain a similar organization, the Provincial Surgical Society, had been formed. Membership in the Society of Clinical Surgery is limited to fifty. This method of informal clinical demonstrations has met with great success, and this society has served as the prototype for many similar organizations or travel clubs, not only in surgery and the surgical specialties but in other fields of medicine as well.

Franklin H. Martin (1857-1935), managing editor of the journal *Surgery, Gynecology and Obstetrics,* which had been established in 1905, impressed by this dramatic method of objective presentation of clinical work, conceived the idea of utilizing such a plan for adult education, on a much larger scale in order to make available to the great group of practicing surgeons the advantages theretofore possible for only a few. At his instigation, the editorial board of *Surgery, Gynecology and Obstetrics* arranged for a group of surgical clinics to be given in Chicago from Nov. 7 to 19, 1910, to which it invited subscribers to the journal. The attendance was large and the success of the venture phenomenal, so much so that those attending the clinics expressed a

desire to perpetuate them. Accordingly, a meeting on permanent organization followed and the name The Surgical Congress of North America was selected. As the popularity of the congress continued during the ensuing years, it became evident that it would be necessary to exercise some control and to limit attendance at the clinics to the registered surgeons and to choose wisely the clinics and clinicians invited to participate. This, in turn, led to the plan of Franklin Martin for a new organization closely allied with the congress through which definite qualifications for membership would be established, thereby elevating the standards of surgery. On May 5, 1913, the American College of Surgeons was officially founded, and in 1917 the two organizations were amalgamated.

With the application of surgical methods to the treatment of disorders of the chest, a new specialty, thoracic surgery, evolved in the early years of the present century, and developments in this field were considerably accelerated by the experiences gained in World War I. The real founder and dean of this specialty in America was Willy Meyer (1858-1932). Born and educated in Germany, Meyer at the age of 26 came to New York, where he had a long and remarkable surgical career. Always intensely interested in the various aspects of cancer, he devised an original plan of radical mastectomy for mammary carcinoma. Unknown to Meyer, Halsted, who had been working on the same problem for a longer time, independently developed an almost identical procedure and anticipated Meyer in the reporting of his results. Realizing the great possibilities for thoracic surgery in the future, in February 1917, Meyer invited twenty New York physicians to meet in his office for the purpose of organizing the New York Society for Thoracic Surgery. One of the purposes of this organization was to lay the foundation for an American Association for Thoracic Surgery. At the next meeting of the American Medical Association, in New York city, June 7, 1917, members of the New York Society invited the leading thoracic surgeons of the country to be their luncheon guests, and at that time the American Association for Thoracic Surgery was officially organized with fifty founder members. Samuel Meltzer, of the Rockefeller Institute, was chosen the first president.

A significant event in the history of this surgical organization has been a deviation from the older policy of limiting membership to surgeons alone. Here, on the contrary, internists, radiologists, endoscopists and others working on thoracic problems in the laboratories of physiology, pathology and bacteriology have been welcomed to membership. Secondly, a novel feature in organization has been the group of associate members in addition to the active, senior and honorary members. These

men are elected for a limited period (five years). During this time an associate member, if properly qualified, may be elected to active membership. At the expiration of this limited period, if not yet qualified for active membership, an associate must either be reelected as such for an additional period or be dropped.

Finally, this new surgical organization, with high standards, stimulating meetings and an outlet of its own for publications, made possible membership to a number of the well trained younger general surgeons who were working in the thoracic field and who were desirous of such an affiliation but who were not yet eligible for membership in the older societies.

In September 1912, Harvey Cushing (1869-1939) became the third Moseley Professor of Surgery at Harvard, succeeding Maurice H. Richardson in this the oldest of the endowed surgical chairs. At the same time he became the first surgeon-in-chief at the new Peter Bent Brigham Hospital. Cushing's pioneer work in the surgical treatment of diseases of the nervous system is too well known to warrant recounting here. Being a firm believer in the importance and educational value of medical meetings, at the time of the clinical congress of the American College of Surgeons in New York in 1919, Cushing proposed to some of his colleagues the formation of a neurosurgical travel club. Thereby as a group they could visit one another at their respective clinics, the meetings to be held once or twice a year. The idea was enthusiastically welcomed, and with ten charter members "The Neurosurgical Club" was formed. These original members were A. W. Adson, Charles Bagley Jr., Harvey Cushing, Charles E. Dowman, Charles A. Elsberg, Charles H. Frazier, Samuel C. Harvey, Gilbert Horrax, Dean Lewis and Ernest Sachs. In March 1920, a meeting was held at the Peter Bent Brigham Hospital, at which time the original name was abandoned and The Society of Neurological Surgeons was officially founded. The first clinical meeting was also held in Boston, Nov. 26 and 27, 1920. The general plan has been similar to that of the Society of Clinical Surgery, an organization in which Cushing throughout his life maintained a deep interest. At each meeting one or more members act as hosts at the hospital where they work. The meetings are held in rotation at the various neurosurgical centers. The number of members has not exceeded forty.

A generation of surgeons has come and gone since Chadwick and Gross and Keyes and Shaffer first disclosed to their intimate friends their visionary plans for a particular national surgical society. During this period of nearly seventy-five years, the population of the country has increased almost threefold and the number of physicians has so multiplied that according to the most recent calculations there is now

in the United States one doctor for every seven hundred and ten persons. Nevertheless, the original restrictions on the size of the senior societies have been adhered to almost literally, and presumably owing to reverence for the wishes of the founders, enlargement of the membership has been jealously guarded. With the passing of the years, the requirements for admission have become more and more stringent, and a candidate must, therefore, be more or less well known and must give evidence of having made some contribution to the advancement of the art and science of surgery. As a result, most of the successful aspirants have reached at least early middle age, and election to membership, often beset by delays, not infrequently comes as a *cum laude* award in recognition of a considerable part of their life's work. Because of the emphasis placed on investigation and education, most of the members hold responsible positions in the medical schools. In reviewing the achievements of these organizations, it is difficult or impossible to estimate fully the value of the benefits which have been derived from the combined efforts of the best medical minds in the country concentrating on their particular scientific problems and working for a common cause.

The three quarters of a century just past has witnessed, in addition to the increases in population and number of physicians, a remarkable increase in the number of hospitals and of well trained surgeons. The latter advance has been due chiefly to the more general adoption by hospitals of the residential system, a German method of graduate training originally transplanted to this country by Halsted and Osler in the early days of the Johns Hopkins University. The junior surgeon of today who has attained and held the post of resident surgeon has, at the age of 30, had an experience in surgery which in the case of many of our distinguished forebears could scarcely have been accumulated during a lifetime of practice. The Central Surgical Association hails these junior surgeons, as for them it was conceived and founded, and in welcoming them to membership it endeavors to offer them the opportunities and privileges with the dignity which they deserve. On the shoulders of these younger surgeons now fall the tasks and duties originally assumed by the founders and founder members. As they take over the responsibility for guiding the destinies of the Association in the future, we can do no better than to restate with slight modification the words of Samuel Gross written nearly seventy years ago when he expressed his hopes for the future of the Association which he founded: "to foster surgical art, science, education and literature, to cultivate good feeling in the profession and to unite prominent surgeons of the country in one harmonious body."

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PHARYNGEAL NEURILEMMOMAS OF CRANIAL NERVE ORIGIN

Medial Displacement of the Internal Carotid Artery as a Diagnostic Sign

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FOUR patients with tumors of the upper cervical cranial nerves have been studied. All the lesions were neurilemmomas, 3 arising from the vagus nerve and 1 from the hypoglossal. All 4 cases presented a syndrome consisting of dysphagia due to pharyngeal compression and pulsation of the tumor due to medial displacement of the internal carotid artery. In addition, there was a paralysis of the vocal cord on the same side in 2 of the patients whose tumor arose from the vagus nerve. This triad of findings enabled us to make a clinical diagnosis of the lesion in the last 2 patients. The cases are being reported because, as far as we can ascertain, this syndrome has not previously been described.

The neurilemmoma is not a common tumor, but it is by no means rare. The importance of these lesions lies in the fact that, whereas they are benign encapsulated tumors which are resectable and surgically curable, they are not infrequently confused with malignant lesions carrying a much worse prognosis. In such instances, patients may be subjected to unnecessarily mutilating surgical procedures, such as amputation of an extremity or an ill advised radical resection or to intensive radiation therapy, or they may be refused treatment for a lesion which is completely curable. These considerations are especially pertinent to neurilemmomas arising in the region of the head and neck, where they are relatively inaccessible, where differential diagnosis includes many clinical entities and where pressure effects of a benign tumor may be serious, owing to obstruction of airway, food passages and circulation. Although a neurilemmoma may arise from the sheath of Schwann of a nerve anywhere in the body, according to Ehrlich and Martin[1] about half of all these tumors surveyed were

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From the Department of Surgery, University of Illinois, College of Medicine, the Illinois Research and Educational Hospitals, and the Presbyterian Hospital.

1. Ehrlich, H. E., and Martin, H.: Schwannomas (Neurilemmomas) in the Head and Neck, Surg., Gynec. & Obst. **76**:577, 1943.

found in the head and neck region, the majority being cervical in location. In only 26 per cent of Stout's series of 50 cases was the tumor found above the clavicles.[2] Ten neurilemmomas have been reported arising specifically from cranial nerves in the cervical region,[3] involving the pharynx. Many cases have been reported in which these tumors arose in the head and neck.

The nomenclature of these benign encapsulated neurogenic tumors is varied, resulting in confusion. Described and termed neurinoma in 1910 by Verocay,[4] subsequent writers have referred to this tumor as a perineural fibroblastoma,[5] neurilemmoma,[6] schwannoma,[7] neurofibroma [8] and peripheral glioma.[9] The terms neurilemmoma and schwannoma are most frequently used, and, since the former seems to be the most accurate designation, it is used here to designate those tumors which have their origin from the neurilemma of cranial and peripheral nerves. Theoretically, neurilemmomas may arise in any part of the body, although they are most frequently found in the cervical region, where the cranial nerves and sympathetic system with cervical plexiform rami are abundant. The anterior aspect of the extremities is the next most frequent location after the cervical region.

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2. Stout, A. P.: The Peripheral Manifestations of the Specific Nerve Sheath Tumor (Neurilemmoma), Am. J. Cancer **24**:751, 1935.

3. (*a*) Turchik, F.: Schwannoma of the Pharynx with Paralysis of the Vocal Cord, Arch. Otolaryng. **44**:568 (Nov.) 1946. (*b*) Cutler, E. C., and Gross, R. E.: Neurofibroma and Neurofibrosarcoma of Peripheral Nerves, Arch. Surg. **33**:733 (Nov.) 1936. (*c*) Nigro, A., cited by Turchik.[3a] (*d*) Murray, M. R.; Stout, A. P., and Bradley, C. F.: Schwann Cell Versus Fibroblast as the Origin of the Specific Nerve Sheath Tumor, Am. J. Path. **16**:41, 1940. (*e*) Bustos, F. M.: Schwannoma of the Pneumogastric Nerve: Case with Recovery after Ablation, Bol. y trab. Acad. argent. de cir. **29**:448, 1935. (*f*) Sekiguchi, S., and Oije, T.: Arch. f. klin. Chir. **143**:113, 1926, cited by Ehrlich and Martin.[1] (*g*) Murley, R. S.: A Case of Neurinoma of the Vagus Nerve in the Neck, Brit. J. Surg. **36**:101, 1948. (*h*) Friedman, L., and Eisenberg, A. A.: Neurofibroma of the Hypoglossal Nerve, Ann. Surg. **101**:834, 1935. (*i*) Ehrlich and Martin.[1]

4. Verocay, J.: Multiple Geschwuelste als Systemerkrankung am nervoesen Apparate, Festschr. f. Mans Chiari. . . . seines 25 jähr. Prof.-Jubil., Wien u. Leipz, 1908, p. 378; Beitr. z. path. Anat. u. z. allg. Path. **48**:1, 1910.

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6. Ewing, J., cited by Ehrlich and Martin.[1] Stout.[2]

7. (*a*) Violé, P.: Schwannoma of the Pharynx, Ann. Otol., Rhin. & Laryng. **55**:334, 1946. (*b*) Koop, C. E.; Jordan, H. E., and Horn, R. C.: Schwannoma of the Pharynx, Surg., Gynec. & Obst. **85**:641, 1947. (*c*) Turchik.[3a]

8. (*a*) Figi, F. H.: Solitary Neurofibroma of the Pharynx, Arch. Otolaryng. **17**:386 (March) 1933. (*b*) Hall, C., and Owens, H.: Solitary Neurofibroma of the Pharynx, ibid. **34**:1163 (Dec.) 1941. (*c*) Cutler and Gross.[3b]

9. Masson, P.: Experimental and Spontaneous Swannomas (Peripheral Gliomas), Am. J. Path. **8**:367, 1932.

Pharyngeal neurilemmoma is relatively uncommon. New and Childrey [10] collected from the Mayo Clinic 63 cases of benign tumors of the pharynx and tonsil over a thirteen year period (1917-1930). In this relatively large group of benign tumors, a primary neurilemmoma of the pharynx was not encountered. Koop, Jordan and Horn [7b] recently collected 6 cases from the literature and contributed 5 of their own. Additional cases of pharyngeal neurilemmoma have been reported by Turchik,[8a] Violé [7a] and others.[11]

There appears to be no common causative factor contributing to the genesis of these tumors, although some authors associate their occurrence with von Recklinghausen's disease. In about 18 per cent of cases, solitary neurilemmomas are found coexistent with frank or suspected multiple neurofibromatosis.[12] Pharyngeal neurilemmomas are encountered about equally in the two sexes between the ages of 20 and 65. In our experience they have all been found in women.

Pharyngeal neurilemmomas when small will remain asymptomatic over a period of many months. The most frequent presenting complaints are the awareness of a mass in the throat and some degree of dysphagia. A neurilemmoma arising from the perineurium of a sympathetic nerve or involving the postganglionic fibers of the superior cervical ganglion may result in a Horner syndrome. Usually this syndrome is encountered more commonly as a transient postoperative complication,[13] but it may persist for months.[14] Segmental cervical root pain is not uncommonly experienced in cases of cervical neurilemmoma but less frequently encountered when the pharynx is involved. Hoarseness and some degree of dysphagia are experienced when the vagus nerve, particularly the medial and external portion containing the special visceral efferent fibers, is involved. Weakness of the ipsilateral shoulder occurs when the expanding neoplasm encroaches on the spinal accessory nerve, disturbing the innervation of the trapezius muscle.[8] Dyspnea is a late sign observed in patients in whom the tumor has assumed large proportions. Ulceration and hemorrhage

10. New, G. B., and Childrey, J. H.: Tumors of the Tonsil and Pharynx (Three Hundred and Seventy-Five Cases): I. Benign Tumors (Sixty-Three Cases), Arch. Otolaryng. **14**:596 (Nov.) 1931.

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12. Stout, A. P.: Neurofibroma and Neurilemmoma, Clin. Proc. **5**:1, 1946.

13. Hill, F. T.: Neurofibroma of the Pharynx with Paralysis of the Larynx Following Operation, Ann. Otol., Rhin. & Laryng. **53**:326, 1944. Nigro.[8e]

14. Turchik.[8a] Violé.[7a]

generally do not occur. On physical examination a tumor mass may be found in the anterior cervical triangle or beneath the sternocleidomastoid muscle, but in any case a bulging of the pharyngeal wall is encountered, usually arising from the tonsillar fossa. The tumor has a slightly movable "rubbery feel" and if large may be cystic. The

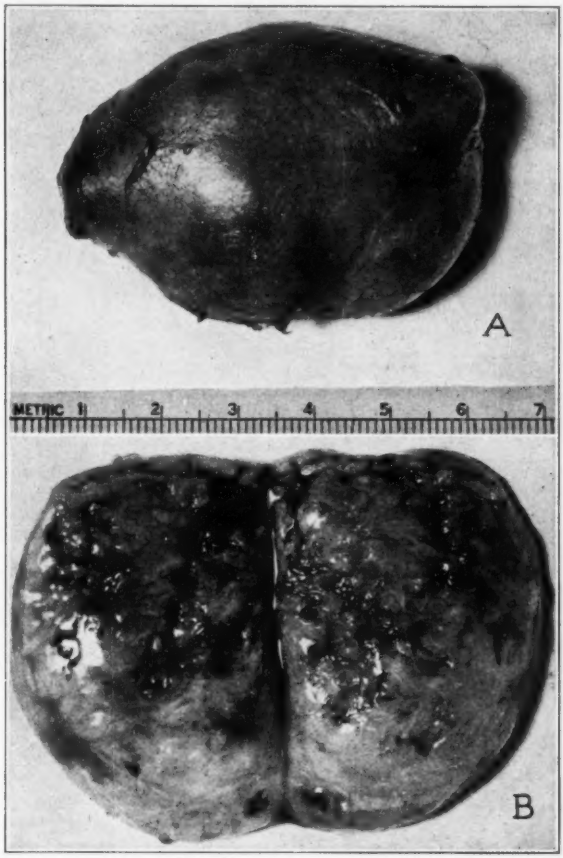

Fig. 1.—*A*, Encapsulated neurilemmoma of the left vagus nerve (case 4). *B*, the sectioned surface is tan-gray and gelatinous. In the central portion hemorrhage, degeneration and liquefaction necrosis are present.

mucous membrane is unattached and may move freely over the neoplasm. The shadow cast in a roentgenogram is not characteristic and cannot be distinguished from the shadow cast by any other soft tissue tumor.

Neurilemmomas are usually solitary encapsulated tumors (fig. 1). The surface is smooth but may be irregularly lobulated. The sectioned surface is brown-gray, resembling the color of a cross section of

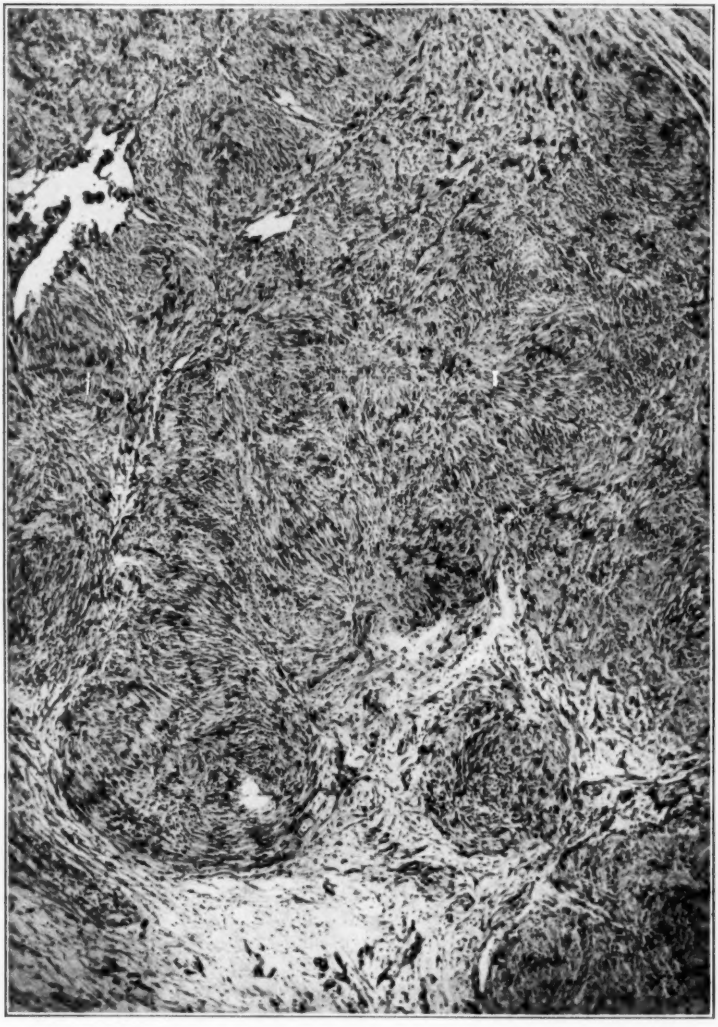

Fig. 2.—Photomicrograph of the tumor in case 3. Type A and B Antoni tissues are seen. "Verocay bodies" composed of palisading schwannian cells are present. Hematoxylin and eosin; × 70.

nutmeg. In the central portion of the tumor, hemorrhage, degeneration and liquefaction necrosis are commonly found. The larger tumors are usually soft and cystic as a result of central necrosis. Central liquefaction necrosis is not observed in neurofibromas, even though the tumor may attain large dimensions.[12]

The histopathology is characteristic, consisting of two types of tissue (fig. 2). Antoni type A tissue is made up of a palisading long-fibered reticulum passing between elongated nuclei. This tissue is compact, in contrast to Antoni B tissue. Occasionally, "Verocay bodies" are found in the Antoni A component. These bodies are composed of highly differentiated schwannian cells with wiry reticulin fibers. Interspersed throughout the A tissue is the loosely textured Antoni B tissue, composed of schwannian syncytium without palisading. In this syncytium are microcysts produced by intracellular edema. These may coalesce and form visible cystic spaces. Hemorrhage and necrosis are found throughout the central portion of the larger neurilemmomas.

The schwannian theory of histogenesis has been strongly favored on the basis of the results of tissue culture studies of Murray, Stout and Bradley.[3d] The cells of these specific nerve tumors are morphologically and physiologically similar to the cells of Schwann.[9]

REPORT OF CASES

CASE 1.—*History.*—E. L. R., a white woman, 65 years of age, was admitted to the hospital complaining of progressive dysphagia, "throbbing" in the throat and dyspnea on lying down, of four years' duration. A slowly growing pharyngeal tumor mass was the cause of her symptoms. An unsuccessful attempt at removal through a lateral cervical incision had been made elsewhere seven months previously. Subsequently she was hospitalized at another institution, where she was considered to have an arteriovenous aneurysm, or "pulsating hemangioma," of the left posterolateral pharyngeal wall. Five radon seeds had been inserted into the tumor.

Examination.—The essential physical findings were the presence of a smooth, bulging tumor mass, firm but not hard in consistency, oval in shape, occupying the left posterolateral portion of the pharynx. The lesion extended superiorly from the vault of the nasopharynx down to the level of the cricoid cartilage. It extended from the median raphe to the anterior tonsillar pillar and occupied half the lumen of the pharynx. The covering mucosa moved freely over the tumor and was infiltrated with numerous small bluish veins. The entire mass seemed to pulsate, but critical examination showed this to be transmitted pulsation from a single large arterial trunk which curved about the medial border of the tumor, mainly in the midline.

Needle exploration of the tumor after local infiltration with procaine hydrochloride proved it to be solid. An aspiration biopsy was done, and the slides were interpreted as schwannoma (by Dr. Frank W. Foote, of New York).

Neurologic examination revealed no abnormalities, and both vocal cords had normal motility. The patient's blood pressure was 230 systolic and 130 diastolic, and there was hypertensive and arteriosclerotic retinopathy.

The patient was obviously a poor operative risk, but excision of the tumor was elected because of the severe and progressive dysphagia and dyspnea.

Operation.—With the patient under intratracheal anesthesia, the left external carotid artery was ligated in continuity through a lateral cervical incision, no exploration being done other than identification of the vessel. Through a transoral approach, the left lateral pharyngeal mucosa was incised from above downward, just posterior to the tonsil, after retraction of the soft palate. Mucosal flaps were developed, and an oval encapsulated tumor mass was exposed. It was in intimate contact with a large arterial trunk coursing over its medial surface. This was retracted to the right, and the tumor was freed by blunt and sharp dissection. As the operation progressed, it became evident that the artery medial to the tumor was the internal carotid. Because of a hesitant spirit, and adhesions following previous operation and irradiation, the tumor was removed in pieces rather than by dissection of the intact capsule. The most inferior fragment of the tumor was found to blend into a nerve trunk, which obviously was the vagus. The internal carotid pulsated freely after removal of the tumor mass.

Postoperative Course.—As the patient reacted from the anesthesia, it was apparent that she had a right hemiplegia. She slowly recovered over a period of twenty days, and paralysis of the left vocal cord was found after speech was resumed. It is our belief that the left cerebral ischemia was due to retraction compression of the left internal carotid artery during the operation and that the left recurrent laryngeal nerve fibers were interrupted by crude dissection of the tumor from the left vagus nerve.

Pathology.—The resected tumor tissue showed the typical microscopic picture of a neurilemmoma of the Antoni type A pattern, with palisading and "Verocay bodies."

Case 2.—*History.*—B. D., a 68 year old white woman, was admitted to the hospital on Jan. 31, 1946, with complaints of pain in the left tonsillar and occipital area and dysphagia of three months' duration.

Examination.—A large smooth, bulging tumor mass was present in the area of the left tonsil, soft palate and lateral portion of the pharynx, extending into the pterygoid space. It encroached on the airway and was palpable in the neck behind and below the angle of the mandible. The overlying mucosa was not implicated and was movable over the tumor. The mass was firm and slightly movable, and a large pulsating artery was present in the medial and posterior aspect of the mass. The aspiration biopsy was reported as showing a picture consistent with the diagnosis of neurilemmoma. External ocular signs and the larynx were normal.

Operation.—With the patient under intratracheal cyclopropane anesthesia, a curved incision was made from the mastoid process below the mandible to the mental region. The bifurcation of the carotid artery was exposed, and the encapsulated tumor mass was found presenting medially and pushing the artery forward. The external carotid, occipital, external maxillary and temporal arteries were ligated and divided to expose the mass. The internal carotid artery was found to be deep and pushed to the midline of the pharynx by the tumor mass. The tumor mass did not arise in the bifurcation of the carotid artery and was not attached to the artery.

The vagus nerve was found spread out over the tumor, and by blunt dissection the mass was enucleated from the lateral pharyngeal space. It was found to extend from the base of the skull down to the left of the bifurcation and was enucleated

without breaking the capsule. It was attached to the hypoglossal nerve and apparently arose from it. This nerve was sectioned and resutured. The wound was closed with interrupted sutures and drains.

Postoprative Course.—The hospital course was uneventful. The patient was discharged on the sixth postoperative day, with paralysis of the left recurrent nerve and some dysphagia which persisted for three months, after which full recovery was noted. External ocular signs remained normal.

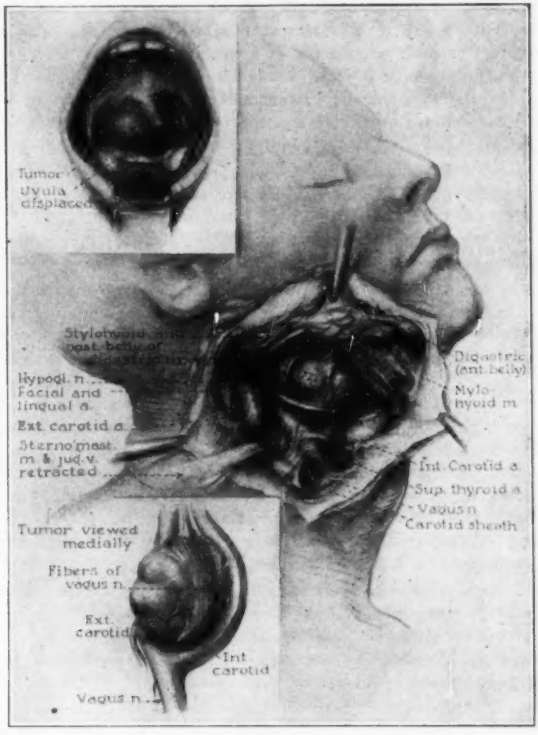

Fig. 3.—Composite and diagrammatic reconstruction of appearance of tumor when exposed through external cervical approach. Upper insert: intraoral view showing bulging tumor mass; lower insert: relationship of vagus nerve to tumor.

Pathologic Examination.—"The specimen consisted of a well encapsulated tumor. On palpation a few nodules were felt. The mass measured 5 by 4 by 2.5 cm. On sectioning, the capsule was gray, measuring 0.1 to 0.2 cm. in thickness. The tumor grossly appeared lobulated, separated by relatively firm gray tissue. A few foci of necrosis were noted as well as areas of hemorrhages. There were yellow areas scattered all over the specimen.

Microscopic examination showed that the tumor was characterized by varied areas; there were cellular fibrillar zones with more or less interwoven bands in areas, combined with palisading. In addition, there were extensive areas of marked edema, other areas of dense fibrosis and, again, areas of frank necrosis. The tumor was highly vascular, and many of the blood vessels were surrounded by hyalinized zones, often containing many fat-laden monocytes. There were also scattered hemosiderin-laden monocytes and scattered areas of round cell infiltration. The tumor was, in all, fairly well confined and revealed no microscopic evidence of frank malignancy. The diagnosis was neurilemmoma.

CASE 3.—*History.*—M. F., a 60 year old Negro housewife, was admitted to the hospital on Aug. 6, 1947, complaining of a mass in her throat with progressive difficulty in swallowing of four years' duration. For the last month there had been obstruction of the airway, and she was admitted to the surgical service on a semi-emergency basis because of stridor and the imminent necessity of tracheotomy.

Examination.—There was a smooth, lemon-sized mass protruding from the right tonsillar fossa, occupying half the pharyngeal space and extending deeply into the hypopharynx. The overlying mucosa was movable and not infiltrated by the tumor. On the posteromedial aspect of the tumor, almost in the midline of the pharynx, a pulsating large artery was present. Direct laryngoscopy revealed flaccid paralysis of the right vocal cord.

Operation (fig. 3).—With the patient under intratracheal anesthesia, a Bastianelli type of incision was made on the right. The sternomastoid muscle and jugular vein were located and retracted posterolaterally, and the underlying tumor mass was exposed. There was marked distortion of the carotid vessels, the external carotid artery with its branches coursing over the external surface of the mass and the internal carotid artery being displaced medially at a sharp angulation. The lower pole of the tumor blended into the vagus nerve, and the mass extended up behind the mandible into the pterygoid space. The stylohyoid muscle and the posterior belly of the digastricus were divided, and the external carotid and interfering branches were ligated and sectioned. The tumor was dissected free rather easily with its capsule intact, without a break in the pharyngeal mucosa and without complete section of the vagus nerve. The nerve fibers were spread over the tumor and could be separated without difficulty.

Postoperative Course.—Recovery was uneventful, and the patient was discharged five days after operation. There was full recovery of her voice. On indirect examination, the larynx was normal. The patient was last seen on July 9, 1948, one year after operation. Her only complaint was occasional lancinating pain in the right mandible and parotid area on eating.

Pathology.—"The specimen consisted of an encapsulated, soft, ovoid mass with a pink-tan, shiny, smooth surface. It measured 7 by 3 by 2.5 cm. and had been previously opened. The cut surface was soft, and heterogenous white, red, brown, yellow-tan and glassy mucoid areas were also seen. On microscopic examination, the section revealed an encapsulated tumor mass composed of rather vascular fibrous tissue in a loosely whorled arrangement with many areas of hemorrhage, degeneration and necrosis. The nuclei were pleomorphic and oval shaped, with a tendency toward palisading and giant cell formation." The diagnosis was nuerilemmoma.

CASE 4.—*History.*—P. M. A., a 53 year old white factory worker, was admitted to the hospital on Nov. 7, 1948, complaining of a "neck tumor" accompanied with hoarseness, dysphagia and pain radiating over the left side of the neck, face and

head. Symptoms had been present for seven years. At another institution, the tumor had been incised and drained twice, yielding "dark green water" and temporarily relieving the patient's symptoms. A tonsillectomy four years prior to her admission did not affect the tumor or alleviate her symptoms. The patient was told that a "ruptured pulsating blood vessel" over the tumor prevented transoral removal.

Examination.—There was an indurated scar beneath the angle of the left mandible. A lemon-sized rather soft tumor mass was found arising from the left tonsillar fossa and extending across to the midline of the pharynx and deep into the hypopharynx. A pulsating vessel lay over the medial border of the tumor beneath the mucosa of the pharynx. The pharyngeal mucosa was hyperemic but freely movable over the tumor. The larynx was edematous and injected. The left vocal cord was paretic. Conditions observed on ocular examination were within normal limits.

Operation.—With the patient under intratracheal thiopental sodium (pentothal sodium®)–ethylene anesthesia, a modified Bastianelli incision was made. The sternocleidomastoid muscle and internal jugular vein were retracted posterolaterally to expose the tumor. The external carotid artery and branches were displaced anteriorly by the tumor, while the internal carotid was displaced to the midline. The tumor arose from the vagus nerve (left) and extended from about the level of the larynx into the pterygoid space to the base of the skull. After division of the stylohyoid muscle and the posterior belly of the digastric muscle, the tumor was extirpated by sharp and blunt dissection. The tumor with its capsule was removed intact without damaging the pharyngeal mucosa. The vagus was not divided but was dissected from the tumor capsule with little difficulty. A transient bradycardia attended the extirpation of the tumor. A rapid recovery of normal cardiac rate occurred after the tumor was removed. The wound was closed with interrupted cotton sutures and drained.

Postoperative Course.—A transient Horner syndrome (left) persisted for forty-eight hours after operation. The patient was discharged on the eighth postoperative day without relief of her hoarseness but with relief of the dysphagia and some of her painful symptoms.

Pathology.—"The specimen consisted of an ovoid tumor which measured 5 by 3.5 by 1.5 cm. (fig. 1). It felt cystic and moderately soft. The surface was covered by a thin capsule. Attached to one portion was a fibrillar structure resembling nerve fiber. The sectioned surface was tan-pink and somewhat gelatinous. In the central portion there were cystic degeneration, hemorrhage and necrosis. Microscopic examination revealed that the tissue was made up of fibroblastic cells arranged in many areas in palisades. There was considerable diversity in the appearance of the various cells. Occasional mitotic figures were observed. In other areas there were hemorrhage and hemosiderin-filled macrophages. A section of nerve tissue was found associated with the fibrous capsule." The diagnosis was neurilemmoma.

COMMENT

These 4 cases have several points in common: The tumors were of relatively slow growth; they produced serious symptoms which would have led to a fatal termination if unrelieved; all 4 were benign, and all were surgically remediable. In 2 of the cases the diagnosis was made by aspiration biopsy. These 4 cases present certain clinical

features which, taken together, should allow a presumptive diagnosis of neurilemmoma of cranial nerve origin. These features are: the presence of a submucosal tumor mass protruding into the posterolateral pharyngeal area; the history of slow growth; the presence of a single large pulsating arterial trunk at the medial limits of the tumor, and evidence of paresis of the vagus, hypoglossal or accessory nerves. The last feature is inconstant, but when it is present with the other features it should fairly clinch the diagnosis. In 2 of our patients interference with a cranial nerve was evident before operation —in these instances the vagus. This feature also has been noted by Turchik.[3a] Medial displacement of the internal carotid artery has been mentioned once as an incidental observation in a case of tumor of the upper portion of the vagus nerve, but in this report pharyngeal symptoms or changes were not described.[3g] Violé [7a] has noted a tendency of the tumor to force the artery outward when the neoplasm was found anterior to the carotid sheath and below the upper third of the sternocleidomastoid muscle.

The tumors which could be most commonly confused with a neurilemmoma of cranial nerve origin are, in order of importance, mixed tumors of salivary gland type arising in mucous glands of the pharyngeal or palatal mucosa, adenocarcinoma of the same origin, lymphosarcoma and "lymphoepitheliomas" of the tonsil without mucosal ulceration, chordomas and tumors of the carotid body. All these tumors should be readily differentiated by aspiration biopsy if an actual smear of tumor tissue is obtained. The microscopic patterns of these lesions are fairly distinct, even on smear. The aspiration biopsy technic [15] should be useful at least in differentiating benign and malignant tumors. On anatomic grounds, none of the tumors mentioned could displace the internal carotid artery medially, except a carotid body tumor, as mentioned in 1 instance by Lahey.[16]

Treatment of pharyngeal neurilemmomas of cranial nerve origin is entirely surgical. Irradiation is not only useless but harmful. It is our opinion that the lateral cervical approach is far better than a transoral one. The principal hazard in excision is hemorrhage, and this can be prevented or controlled much more easily by a wide exposure, identification and retraction of vulnerable vessels and their dissection under direct vision. The pharyngeal mucosa can be dissected free without penetration, permitting the operative procedure to be done without contamination, a maneuver impossible to achieve

15. Martin, H. A., and Ellis, E. B.: Aspiration Biopsy, Surg., Gynec. & Obst. **59**:578, 1934.

16. Lahey, F. H., and Warren, K. W.: Tumors of the Carotid Body, Surg., Gynec. & Obst. **85**:251, 1947.

by the transoral route. Actually the dissection of these tumors by the external approach is easier than might be imagined because of the displacement of important structures by the tumor.

A neurilemmoma may occasionally show malignant tendencies, metastasizing [3b] and revealing a microscopic picture with abnormal giant cells and mitoses.[17] Furrer and Fox [18] have published a case of perineural fibrosarcoma of the left vagus sheath metastatic to the tail of the pancreas. The presenting clinical findings were progressive hoarseness and dysphagia and on the left cervical pain and Horner's syndrome. Evidence of a cervical tumor was not conclusively established until the last few months of the patient's illness.

Neurilemmomas if completely excised do not locally recur. Pharyngeal neurilemmomas, potentially malignant, destroy locally by expansion and pressure necrosis. For these reasons they should be extirpated.

SUMMARY

The clinical findings and surgical management of 4 patients with neurilemmomas originating in the upper cervical cranial nerves are described. Three of these tumors arose from the vagus nerve and 1 from the hypoglossal.

Certain features common to all 4 cases would seem to allow a clinical diagnosis of such lesions. These are: (1) a bulging, firm submucosal tumor mass presenting in the posterolateral pharyngeal wall, causing dysphagia and, later, interference with the airway; (2) pulsation of the tumor mass, due to medial displacement of the internal carotid artery, and (3) interference with function of the nerve involved. Two of the patients with tumors of the vagus nerve had paralysis of the vocal cord on the same side.

Extirpation of these lesions is best done through an external cervical approach.

17. Foot, N. C.: Pathology in Surgery, Philadelphia, J. B. Lippincott Company, 1935, pp. 438-441.

18. Furrer, E. D., and Fox, F. R.: Perineural Fibrosarcoma of the Left Vagus Sheath: Report of a Case, West. J. Surg. **48**:584, 1940.

TREATMENT OF THE "SHOCK KIDNEY"

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DETROIT

SHOCK may be defined as a condition of acute prolonged depression of blood pressure and circulating blood volume. Among the conditions in which it occurs are anaphylaxis, coronary occlusion, poisonings of various kinds, overwhelming infections and, most important from our standpoint, trauma and hemorrhage.[1]

This is not the place to discuss the various theories of the mechanism of traumatic shock, or to attempt to detail or analyze the great confusing mass of experimental and clinical observations which continue to appear in the literature. It is enough to say that there are three theories of the underlying mechanism of traumatic shock: first, that it is of predominantly nervous origin; second, that there is produced by trauma a circulating vasodepressor substance, and, third, that it is due to loss of blood, either externally or internally into the tissues. At present, the consensus is that though the nervous system and a circulating depressor substance may be factors, the primary cause in practically all cases of traumatic shock is hemorrhage.[2]

The "shock kidney" is the renal condition which may accompany or follow prolonged, profound circulatory depression; it is characterized by oliguria or anuria, increasing azotemia, and, usually, the presence of heme casts in whatever urine may be excreted.[3]

The clinical aspects have long been known, and the pathologic features have been described in the past, but it has been only in the last decade that confusion has been dispelled and the clinical and

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Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Moon, V. H.: Shock: Its Dynamics, Occurrence, and Management, Philadelphia, Lea & Febiger, 1942.

2. (*a*) Freeman, N. E.: Newer Concepts of the Pathologic Physiology of Shock, S. Clin. North America **26**:1319, 1946. (*b*) Gregersen, M. I., and Root, W. S.: Experimental Traumatic Shock Produced by Muscle Contusion with a Note on the Effects of Bullet Wounds, Am. J. Physiol. **148**:98, 1947. (*c*) Moon, V. H.: The Pathology of Secondary Shock, Am. J. Path. **24**:235, 1948. (*d*) Swindler, C. M.: Hemorrhagic Shock, Am. J. Surg. **76**:182, 1948.

3. Moon, V. H.: Renal Deficiency Associated with Shock, J. A. M. A. **134**:425 (May 31) 1947.

pathologic features coordinated into a clear, though still somewhat provisional, picture on which a rational plan of treatment can be based.

The clinical observations and pathologic studies made by Byswater, Mallory,[4] Lucke[5] and others during and after the war on persons dying after battle injuries or from crush injuries, supplemented by experimental and clinical observations by Trueta,[6] Corcoran and Page,[7] Thorn, Van Slyke[8] and others, have brought about the present conception.

To this renal condition Lucke, has given the name "lower nephron nephrosis," which has been widely adopted. Like all labels, it can be used as a substitute for thinking, and undoubtedly in individual cases important conditions of the kidney have been masked by the mere application of this label. Synonyms are prerenal azotemia, hepatorenal syndrome and hemoglobinuric nephrosis.

The condition is not peculiar to shock, and, in fact, is seen more frequently in other circumstances. Among the commoner exciting causes are intravascular hemolysis associated with transfusion reactions; heatstroke; uteroplacental damage; after abortion; sulfonamide sensitivity, and from various poisons, notably carbon tetrachloride.[2c]

It is probably never seen completely uncomplicated by lesions in other organs, but the complications are much less in evidence in some of the cases of the mild toxic form, such as those associated with pregnancy, intravascular hemolysis and sulfonamide sensitivity, than in the cases associated with traumatic shock. Even in the cases of the mild toxic condition, however, some hepatic damage is undoubtedly present, and in cases of shock there is reason to believe that a biochemical lesion of the liver is responsible for the rapid deterioration of the shock state, for damage to the kidney and adrenal gland is not immediately important, since loss of function there is not so rapidly lethal.[9]

Typically the affected kidney has the following gross characteristics: It is large, smooth and pale; on cutting, the cortex is pale and the

4. Mallory, T. B.: Hemoglobinuric Nephrosis in Traumatic Shock, Am. J. Clin. Path. **17**:427, 1947.

5. Lucke, B.: Lower Nephron Nephrosis, Mil. Surgeon **99**:371, 1946.

6. Trueta, J.; Barclay, A. E.; Daniel, P. M.; Franklin, K. J., and Prichard, M. M. L.: Studies of the Renal Circulation, Springfield, Ill., Charles C Thomas, Publisher, 1947.

7. Corcoran, A. C., and Page, I. H.: Crush Syndrome: Post-Traumatic Anuria, J. A. M. A. **134**:436 (May 31) 1947.

8. Van Slyke, D. D.: The Effects of Shock on the Kidney, Ann. Int. Med. **28**:701, 1948.

9. Fine, J.; Seligman, A. M., and Frank, H. A.: On the Specific Role of the Liver in Hemorrhagic Shock, Ann. Surg. **126**:1002, 1947. Shorr, E.: Hepato-Renal Factors in Traumatic and Hemorrhagic Shock, Bull. Johns Hopkins Hosp. **81**:70, 1947.

medulla is congested and has prominent striations. Microscopically the glomeruli appear essentially normal, the chief lesion being necrosis of the cells of the distal convoluted tubules and the ascending or thick limb of the loop of Henle, with heme casts in the tubules (fig. 1).

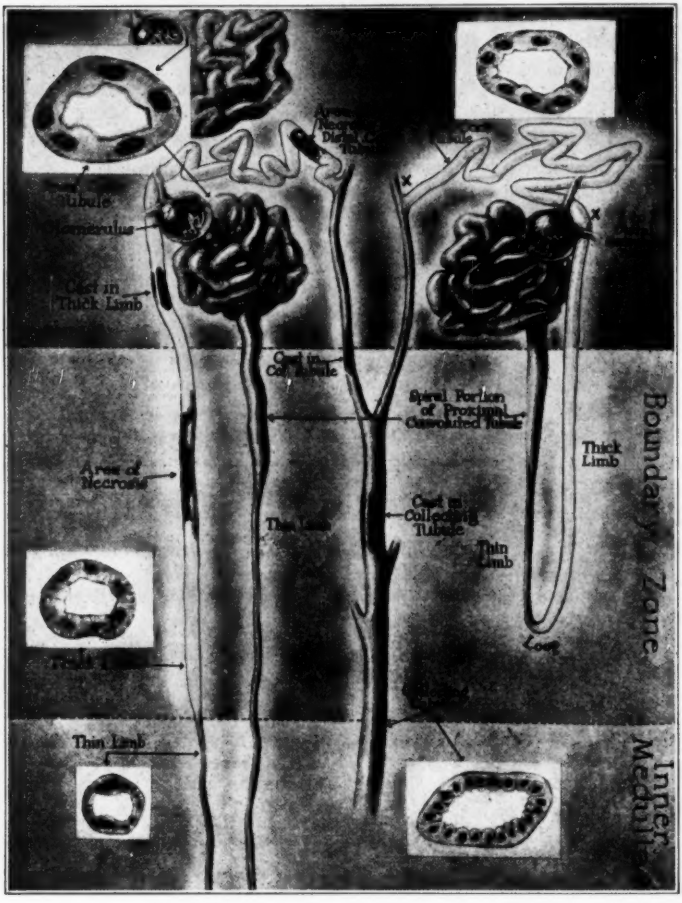

Fig. 1.—Structure of the normal nephron and site of the lesion in lower nephron nephrosis. (From Lucke.[5])

This is a simplified or typical picture. Of course it may be engrafted on any previously existing renal disease, and it is probable that further progress of the agent or condition producing it may cause more exten-

sive lesions involving the proximal portions of the nephron even including the glomerulus.

Theoretically in shock these lesions are brought about by anoxia. As a matter of fact, the early effects of toxins and of anoxia on the liver and kidney cells are indistinguishable and there is good reason to believe that toxic substances act on these cells by inciting anoxia, and the longer the anoxia persists the more extensive should be the injury.

The kidney apparently ranks with the liver in the ability to withstand anoxia—not so vulnerable as the brain but more so than skeletal tissues. Therefore there should be a stage in which if the anoxia is ended no damage to the kidneys would be observed, and clinically this is the case. In other words, the damage is a function of the time of action of the cause. Mallory [4] concluded that the successive stages of the lesions were as follows: (1) within twenty-four hours lipid vacuolation of the cells of the ascending limb of the loop of Henle; (2)twenty-four to seventy-two hours after injury precipitation of heme casts in distal tubules and (3) occasionally on the third and regularly on the fourth and fifth days, necrosis and regeneration of the epithelium of the ascending limb and distal tubules. When the damage is at its height, the tubules lose their ability of selective resorption and any filtrate received by them from the glomeruli is poured back into the blood stream.

Before the present conception of the course of events, the thinking regarding the process going on in the kidney and the proper way to handle it was rather foggy. There was a vague idea that the glomeruli required stimulation and that the tubules were blocked by the heme casts; so the accepted treatment was the attempt to simulate the glomeruli and wash out the plugging casts by the pouring in of vast quantities of fluid—with the common result, since fluid was not being eliminated by the kidneys, that the circulation became overloaded and insufficient, and death too often occurred with pulmonary edema. This is not to say that this circulatory embarrassment was the invariable or sole cause of death. In many cases extensive hepatic damage was found to be present. Experience has shown that the renal lesions are reversable and that if the toxin or other deleterious substance is eliminated, normal circulation restored and the life of the patient preserved long enough, the tubular cells will regenerate and reassume their normal function. Mallory observed regeneration as early as the fourth day after injury.

Oliguria and anuria are spectacular, attention-arresting, phenomena and in the past have held too alarming a place in the mind of the

surgeon. Moreover, the dangers of azotemia have been exaggerated. On record are the patients who have lived more than three weeks after a solitary kidney was removed and in everybody's experience is the patient with chronic renal disease, polycycstic or otherwise, who lives an active life for months in spite of azotemia.

Particularly in the early stages, the danger of anuria or oliguria is not that of poisoning by the products of metabolism but of retention of fluids and imbalance of electrolytes and carbon dioxide.

The treatment of shock kidney can be considered under four heads: prevention; maintenance of fluid balance; maintenance of electrolyte balance, and treatment of azotemia.

1. *Prevention.*—Prevention of shock kidney consists in averting the loss of blood volume and pressure by the giving of blood and fluids before it takes place, or in restoring volume and pressure by the same means as soon as possible after it takes place. This must be done with discretion. Often the vascular system has been treated as if it resembled a somewhat leaky rigid vessel, and the attempt has been made to fill it to a certain mark—namely, normal blood pressure. It may be that a more useful comparison would be with a distensible vessel like the bladder, the overstretching of which may cause paralysis. So in the attempt to prevent or remedy shock probably not much more fluid (blood, plasma, etc.) should be given than will replace estimated blood volume loss. It is difficult to estimate the amount of blood loss and to determine the rate and the amount of transfusion under emergency conditions. Undoubtedly more patients have been saved by transfusions than have been drowned by too much blood, but the following 2 cases are suggestive.

Case 1.—A man of 53, during operation for carcinoma of the cecum, received 1,000 cc. of blood, the blood pressure remaining stable throughout. After operation the urinary output per day, except on one day, did not exceed 325 cc., and it was calculated that the patient received an average of about 200 cc. of fluid per day above his total output. His nonprotein nitrogen level rose steadily till his death, on the thirteenth postoperative day. On the tenth day his blood pressure rose and signs of pulmonary edema appeared. Postmortem examination showed the lesions of lower nephron nephrosis superimposed on nephrosclerosis and early pyelonephritis. There was severe pulmonary edema and no hepatic damage.

Case 2.—A 52 year old man was admitted with traumatic rupture of the left kidney, rupture of the spleen and fracture of two ribs. His condition improved with blood transfusions, and twenty-four hours after admission the left kidney and the spleen were removed. During operation he received 1,500 cc. of blood and his blood pressure remained on a satisfactory level. Shortly thereafter it fell so low as to be unobservable, and in the course of three hours he received an additional 2,500 cc. of blood. His blood pressure rose above the level it had held during operation, signs of pulmonary edema appeared, and he died two hours later. Autopsy showed only pulmonary edema and no fresh hemorrhage.

2. *Maintenance of Fluid Balance.*—In the presence of continued oliguria or anuria, only the amounts of fluid lost through perspiration, respiration and vomiting and through the bowels should be replaced. If no vomiting, diarrhea or profuse sweating occurs, the insensible loss is somewhere around 1,200 cc. a day.

Oliguria occurs commonly after operation, either on a nervous basis or owing to temporary lowering of the blood pressure (Trueta's description of a "shunt" of blood around the glomeruli is interesting in this connection). Such oliguria does not necessarily indicate renal damage, as is illustrated by the following case.

CASE 3.—A 52 year old man underwent a two stage thoracolumbar sympathectomy for hypertension. Before operation his blood pressure was 250 systolic and 110 diastolic. After the first stage it was 200 systolic and 110 diastolic. During the second stage the blood pressure fell to imperceptible levels but was restored by the use of vasoconstrictors and the giving of blood and fluids. After operation it fell to 80 systolic and 40 diastolic, and there was associated oliguria with a nonprotein nitrogen content of 62 mg. per hundred cubic centimeters. In the next four days the blood pressure gradually rose to 150 systolic and 90 diastolic, the urinary output increased from 200 cc. to 1,550 cc. and the nonprotein nitrogen fell from 62 to 37 mg. per hundred cubic centimeters.

However, if oliguria persists, it means renal damage. The time at which such damage can be assumed is indefinite, though Mallory [4] stated that it is less than one day. The following case illustrates the rapidity with which the typical renal lesions may develop.

CASE 4.—A man of 45 underwent a difficult and lengthy operation for recurrent islet carcinoma of the pancreas. The blood pressure fell sharply during operation. Oliguria and rapidly increasing azotemia were observed during the three days he lived. Autopsy showed the typical lesions of advanced lower nephron nephrosis as well as acute parenchymatous degeneration of the liver and pulmonary edema.

3. *Maintenance of Electrolyte Balance.*—The sodium chloride content and carbon dioxide–combining power of the blood should be watched. Chlorides and sodium are not difficult to regulate by means of intravenous infusion or by diet. Acidosis is more difficult to remedy and in some cases yields to none of the usual methods of control.

Very appreciable amounts of salt are removed in the perspiration and by the urine after diuresis starts, but, in our experience, with the toxic lower nephron nephrosis no extraordinary measures have been necessary. There have been some observations on potassium levels, but their importance has not been determined.

4. *Treatment of Azotemia.*—Moderate levels of azotemia need cause no alarm. Even though deaths have occurred in association with azotemia levels of less than 100 mg. of nonprotein nitrogen per hundred cubic centimeters of blood, deaths in such cases have usually been due to other causes and severe hepatic damage was present in most. At what level azotemia begins to be dangerous is difficult to say. Cer-

tainly recovery has taken place after the nonprotein nitrogen level reached over 200 mg. per hundred cubic centimeters of blood, but probably some means of elimination are desirable before that figure is reached.

Sweating is an old and somewhat effective method for removing both fluid and nitrogen. It must be kept in mind that a good deal of salt is removed at the same time.

Many years ago Abel, Rountree and associates [10] and, more recently, Murray, Kolff and Alwall [11] have independently developed artificial kidneys and used the instruments in human patients. Efficient operation was made possible, first, by the production and purification of heparin so that the blood could be maintained in a liquid state outside the body and, second, by the development of suitable cellophane tubing through which dialysis could be accomplished. The underlying principles of all types are the same. A thin layer of heparinized blood is run through the cellophane tubing. Surrounding the tubing is the "rinsing" solution, which contains salts to approximate normal plasma —chlorides of sodium, potassium, calcium and magnesium; sodium hypophosphate and bicarbonate, and glucose. Through the dialyzing membrane pass diffusible materials from the blood which are in greater concentration than in the rinsing solution—most significantly the end products of nitrogen metabolism and other toxic materials usually excreted by the kidneys. The originators of the artificial kidney have reported spectacular instances in which it was used to tide patients over the critical period in cases of renal suppression until certain renal elements could regenerate and resume normal excretory function.

The apparatus is rather cumbersome and uncertain, however, and may cause hemorrhage or clotting. We have seen it used vainly in 2 of our cases, and it may have contributed to the fatal result in 1.

Favorable results have been reported with peritoneal perfusion.[12] In the literature are reports of about a hundred cases. We have never

10. Abel, J. J.; Rountree, L. G., and Turner, B. B.: On the Removal of Diffusible Substances from the Circulating Blood of Living Animals by Dialysis, J. Pharmacol. & Exper. Therap. **5**:275, 1913-1914.

11. Alwall, N.: On the Artificial Kidney: I., Acta med. Scandinav. **128**:317, 1947; Clinical Extra-Corporeal Dialysis of Blood with Artificial Kidney, Lancet **1**:60, 1948. Kolff, W. J.: The Artificial Kidney, J. Mt. Sinai Hosp. **14**:71, 1947. Thalheimer, W.: Experimental Exchange Transfusions for Reducing Azotemia: Use of Artificial Kidney for This Purpose, Proc. Soc. Exper. Biol. & Med. **37**:641, 1937. Murray, G.; Delorme, E., and Thomas, N.: Development of an Artificial Kidney, Arch. Surg. **55**:505 (Nov.) 1947.

12. Frank, H. A.; Seligman, A. M., and Fine, J.: Treatment of Uremia After Acute Renal Failure by Peritoneal Irrigation, J. A. M. A. **130**:703 (March 16) 1946. Seligman, A. M.; Frank, H. A., and Fine, J.: Treatment of Experimental Uremia by Means of Peritoneal Irrigation, J. Clin. Investigation **25**:211, 1946.

used it after shock but have used it in 2 instances of azotemia, one being terminal nephritis. In both it seemed to function well and substantial amounts of nitrogen were found in the perfused fluids, and in both cases by its use the azotemia either diminished or was stablized. It is simple to install. Our method was to introduce a Pezzar catheter into the peritoneal cavity high in the right flank for intake and a sump drain in the left lower quadrant for outlet. The chief drawback was

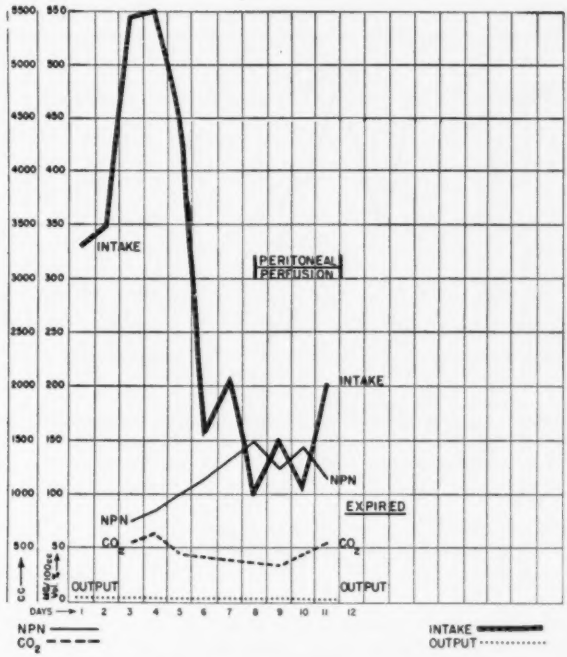

Fig. 2.—Chart from a fatal case of sulfadiazine poisoning, showing the effect of peritoneal perfusion on the nitrogen level. The apparatus was in operation between the fourth and twelfth days, during which the nonprotein nitrogen level of the blood fell, in spite of the fact that the urinary output remained stationary at a low level. On four occasions the nonprotein nitrogen level of the perfusing fluid varied between 64.5 and 131 mg. per hundred cubic centimeters. This patient received too much fluid in the early days of his treatment and died with pulmonary edema. There was also hepatic damage.

that it required the full time attention of someone—nurse or physician —to toy with the outlet tube to keep the fluid running, for the omentum has a tendency to wind itself about the outer tube of the drain. It

was interesting to see how by altering the constitution of the perfusing fluid alterations in blood chemistry could be brought about.

Acute peritonitis has been reported to follow use of this method. Both our patients died, and autopsy showed no acute peritonitis but did show opacity and thickening of the peritoneum, suggesting that the period of effectiveness of such perfusion might be limited. The accompanying charts show the effect on the blood and the amounts of nitrogen withdrawn (figs. 2 and 3).

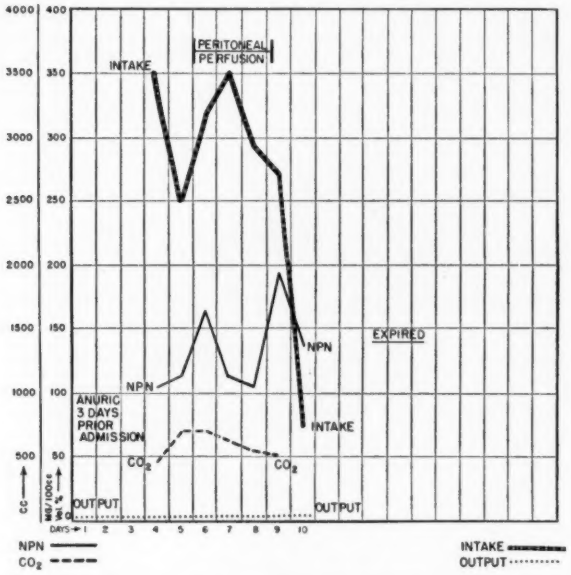

Fig. 3.—Effect of peritoneal perfusion on the nitrogen level in a terminal case of nephritis. During the application of peritoneal perfusion the nonprotein level of the nitrogen of the blood fell. On four occasions the nonprotein nitrogen level of the perfusing fluid varied between 68 and 115 mg. per hundred cubic centimeters.

In a few instances of azotemia we have used gastric and duodenal lavage and were favorably impressed.[13] We were able to diminish or stabilize the nonprotein concentration of the blood, and we could add or extract fluid or salt. Our rather small experience leads us to prefer this method to the others (fig. 4).

Other procedures which have been recommended in the treatment of certain types of anuria—renal decapsulation, spinal anesthesia and

13. Vermooten, V., and Hare, D. M.: The Use of Continuous Gastric Lavage in the Treatment of Uremia Associated with Prostatism, J. Urol. **59**:907, 1948.

paravertebral block [14]—seem to have no place in the presence of, or following, shock. However, renal diathermy is certainly harmless and might well be tried.

The paradoxic conclusion that we reach, therefore, is that the treatment of the "shock kidney" consists in not treating the kidney. Treatment should be directed toward keeping the patient alive. If the patient lives long enough, regeneration of the renal cells will take place. In the over-all picture, the importance of the renal lesion consists in the fact that normal elimination is absent and the realization of this fact must be a controlling factor in the treatment of the patient.[15]

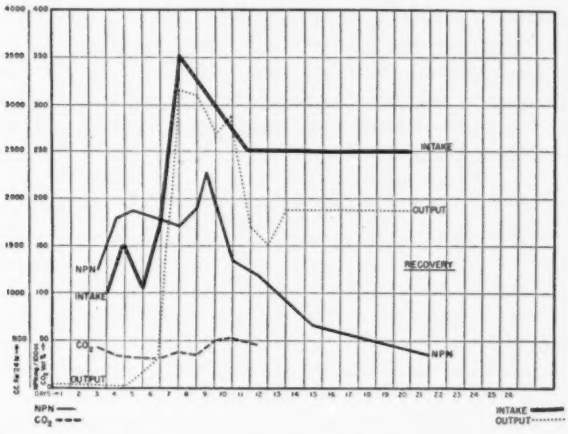

Fig. 4.—Chart of a patient with lower nephron nephrosis due to sulfadiazine poisoning. Gastric lavage was used between the fourth and seventh days, and the chart shows clearly that the nonprotein nitrogen level of the blood did not rise, though the urinary output remained low. On one of these days the gastric washings contained 66 mg. of nonprotein nitrogen per hundred cubic centimeters. On the seventh day the urinary output rose noticeably, and gastric lavage was discontinued; interestingly, the nonprotein nitrogen level rose for several days. This is a common observation in such cases after diuresis begins; the rise may be due to release into the blood of nitrogen which has accumulated in the tissues.

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14. Trimble, I. R., and Sanford, M. C.: Relief of Renal Colic and Renal Suppression: A Preliminary Report, J. Urol. **55**:4, 1946. McGowan, J. M., and Autry, D. H.: Reflex Anuria: Its Treatment by Procaine Sympathetic Block, Am. J. Surg. **76**:205, 1948. Margraves, R. O., and Bogen, E.: Spinal Anesthesia in the Treatment of Reflex Anuria, Urol. & Cutan. Rev. **49**:279, 1945. Cubitt, A. W.: The Problem of Anuria, Brit. J. Surg. **24**:215, 1936.

15. Muirhead, E. E., and Hill, J. M.: The Treatment of Acute Renal Insufficiency, Surg., Gynec. & Obst. **87**:445, 1948. Strauss, M. B.: Acute Renal Insufficiency Due to Lower Nephron Syndrome, New England J. Med. **239**:693, 1948.

CONCLUSIONS

1. Surgical shock is usually due to hemorrhage.

2. The lowered blood pressure of shock may cause damage to the kidney due to anoxia.

3. This damage is reversible if the patient can be kept alive long enough.

4. Treatment at first, therefore, is the treatment of shock—namely, restoration of normal blood pressure and effective blood volume.

5. Replacement of the estimated blood loss is preferable to the attempt to restore blood pressure by unlimited transfusions.

6. After the patient has recovered from shock, if the kidneys are not functioning only enough fluids and electrolytes should be given to replace the fluids and electrolytes lost.

7. If azotemia mounts to dangerous levels, some means of reducing it should be used. In our experience, gastric and duodenal lavage have proved satisfactory.

TRANSPLANTATION OF THE SPINAL CORD FOR PARAPLEGIA SECONDARY TO POTT'S DISEASE OF THE SPINAL COLUMN

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THE PARAPLEGIA resulting from Pott's disease may occur in any stage of the disease and may be a result of several factors. Butler,[1] in a thoroughly studied series of cases, found the incidence of paraplegia in all stages of the disease to be 11.4 per cent. Other authors have cited figures of from 5 to 20 per cent as the incidence of paralysis in this disease. The results of treatment vary somewhat with the extent and neurologic type of the paralysis, the cause of the paralysis and the method of treatment.

It is evident that there are many pros and cons concerning the use of a surgical attack for the relief of paralysis due to tuberculous abscesses and granulation tissue, compression of the spinal cord by pathologic fractures of vertebral bodies, vascular and toxic disturbances of the spinal cord incident to tuberculous disease and the formation of bony ridges causing compression of the spinal cord. All these conditions may occur in connection with Pott's disease.[2]

Laminectomy for the relief of compression of the spinal cord is not without danger. The general health of the patients is not usually of the best. Laminectomy may mean a further weakening of an already weakened spinal column and the possibility of increasing the paralysis due to pathologic dislocations and of causing additional compression of the cord. It carries with it the risk of spreading the infection either locally or by a usually fatal tuberculous meningitis. In spite of these

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Dr. Love is from the Section on Neurologic Surgery, Mayo Clinic.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Ohio, Feb. 18, 1949.

1. Butler, R. W.: Paraplegia in Pott's Disease, with Special Reference to the Pathology and Etiology, Brit. J. Surg. **22**:738-768 (April) 1935.

2. (*a*) Seddon, H. J.: Pott's Paraplegia: Prognosis and Treatment, Brit. J. Surg. **22**:769-799 (April) 1935. (*b*) Seddon, H. J., and Alexander, G. L.: Discussion on Spinal Caries with Paraplegia, Proc. Roy. Soc. Med. **39**:723-734 (Sept.) 1946. (*c*) Butler.[1]

considerations, it appears that a surgical attack has some place in the management of the paralysis occurring in this disease.

Paraplegia accounted for 50 per cent of the paralysis in one group of cases of Pott's disease which has been reported.[2b] This type of paralysis occurs late in the disease. Classically the patient has considerable deformity but has been getting along well after being treated for Pott's disease until he begins to experience some difficulty in walking. This may progress rather rapidly to a complete and total motor paralysis, from which recovery may be either slow or impossible. If recovery does take place, it occurs only after prolonged conservative treatment.

This late paraplegia has been considered to be due to the formation of a bony ridge and the further compression of the spinal cord or to interference with an already precarious blood supply to the adjacent cord. Butler recently stated that the paraplegia was due to the reactivation of the tuberculous process with the formation of granulation tissue and debris in the canal.

Inasmuch as there is interference with the conductivity of the cord regardless of the cause in this late stage, removal of the mass and decompression of the cord seem indicated as soon as paralysis becomes evident and especially if it progresses slowly.

Because of the marked angulation of the vertebral column found in this late stage, a procedure designed to free the cord of its compression and also to allow it to assume a more normal relationship seems to be preferable to a simple decompressive laminectomy. Hyndman [3] in 1947 described a technic for both anterior and lateral transplantations of the spinal cord in cases in which marked kyphosis or scoliosis existed. He reported 2 cases in which these procedures were used. It was his belief that in the majority of cases granulation tissue was the cause of the paralysis and that this procedure had no special application in the treatment of tuberculous kyphosis with signs referable to the cord. He also called attention to the use of anterior transplantation of the spinal cord for acute injuries followed by rapidly developing paralysis.

The possibility of offering patients with paraplegia secondary to bony compression of the spinal cord some chance of a reasonably useful life prompted the use of this procedure in 5 cases which are reported herein.

REPORT OF CASES

CASE 1.—The patient, a married man 28 years old, was seen at the Mayo Clinic on April 24, 1947, because of numbness and weakness in both legs. He gave the history of having fallen when 15 years old and striking the middle of his back. He ached for a few days, and then his symptoms vanished. Six months later he noticed sagging of his left shoulder. He was operated on at a hospital

3. Hyndman, O. R.: Transplantation of the Spinal Cord: the Problem of Kyphoscoliosis with Cord Signs, Surg., Gynec. & Obst. **84**:460-464 (April) 1947.

in his locality (the procedure was unknown), and he was then in a body cast for one year. After the cast was removed, he noticed marked angulation of his back. He was advised to wear a brace for two years. He remained well until nine days prior to admission to the clinic, at which time he noticed spontaneous onset of weakness in both legs which progressed so that two days prior to registration he was unable to walk. Lumbar puncture elsewhere was unsuccessful. Nothing else of significance was noted in his medical or family history. He had been married for one year and was the father of a child.

Physical examination on admission showed marked kyphoscoliosis; the kyphosis was most pronounced in the lower part of the thoracic region. Neurologic examination showed a loss of sensation for pain and touch below the level of about the tenth thoracic segment (fig. 1) and a marked loss of motor power

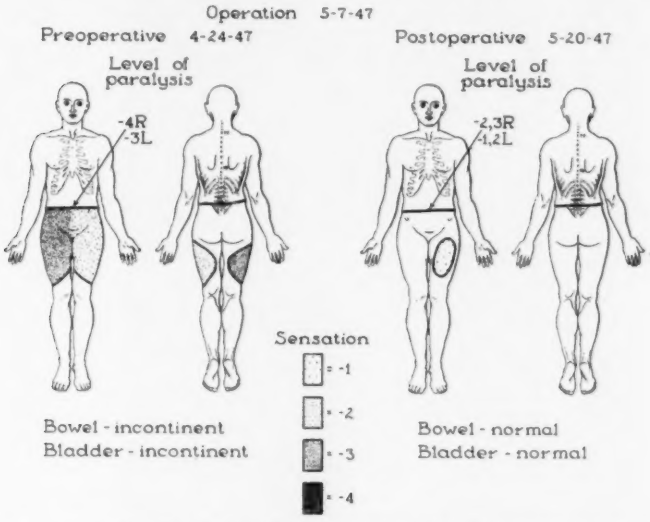

Fig. 1 (case 1).—The principal neurologic findings before operation and immediately after operation. The comparison of the drawings on the right with those on the left show the marked improvement which occurred after transplantation of the spinal cord.

below the first lumbar segment. Reflexes were noticeably increased in the lower extremities, and the patient had bilateral Babinski signs. He had some difficulty in voiding and defecating. An examination of the urine showed an occasional pus cell, but the concentration of hemoglobin, leukocyte count and results of flocculation tests were normal. Roentgenologic examination (fig. 2) revealed an extreme kyphoscoliosis of the thoracic portion of the spinal column, with the kyphosis most marked in the lower portion of the thoracic region. It was felt that the patient had an old Pott's disease of the thoracic portion of the spinal column.

He was hospitalized and placed in traction, but in five days his paraplegia had progressed so that he could no longer move his right foot and his bowels and bladder were completely uncontrollable.

On May 7, 1947, with the patient under general anesthesia, one of us (J. G. L.) performed an exploratory operation. The kyphos was explored from the fifth thoracic to the third lumbar vertebra. The bony portion of the kyphos was smooth and well fused, so that it was not possible to determine where one lamina began and another ended. When the apex of the kyphos was opened with a cranial burr, dense granulation tissue was encountered which covered the spinal cord. A large amount of pus and necrotic material also were found in this region.

Fig. 2 (case 1).—The spinal column after operation showing the marked kyphosis and the silver clips placed on one of the divided nerve roots in the apex of the kyphos (lateral view).

The laminectomy was extended downward on each side of the apex of the kyphos to give exposure beyond the extent of the extradural granulation tissue. Several extradural abscesses were evacuated in the process. As the granulation tissue was removed, pulsations, which had not been evident before, could be seen in the spinal cord over the apex of the hump. The dura was not opened. Inasmuch as the cord still appeared to be tense in spite of the evacuation of much extradural debris, two nerve roots were divided on the left and one on the right (fig. 3).

This allowed mobilization of the spinal cord so that the bridge of bone anterior to the cord, which was producing the angulation, could be removed. Gelatin sponge soaked in thrombin was used to control the bloody oozing along the bony edges. The wound was then closed in layers without drainage.

The pathologic diagnosis of the removed tissue was tuberculous granulation tissue and caseous material.

For two days following the operation, the patient's temperature remained at 101 F., after which it became normal. He required catheterization for nine days after operation, and the sutures were removed on the ninth day.

Neurologic examination fourteen days after operation (fig. 1) showed sensation to be almost intact with some improvement in the right leg and definite improve-

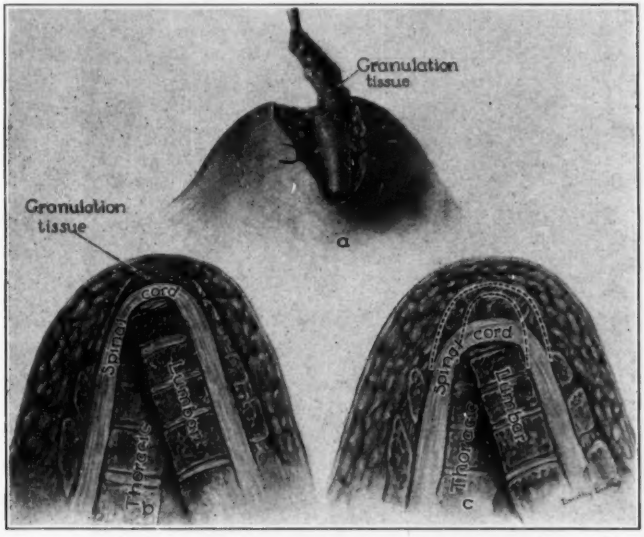

Fig. 3 (case 1).—The condition present and the surgical procedure which was carried out to relieve the compression of the spinal cord. (*a*) Removal of the extradural granulation tissue and ligation and division of nerve roots. (*b*) Sagittal plane showing the marked kyphosis and angulation and compression of the spinal cord between the granulation tissue and the diseased bone. (*c*) The spinal cord transplanted to a new position and thus relieved of pressure.

ment in the motor power of the left leg. In general, the examiner was of the opinion that considerable improvement had taken place. The patient was dismissed from the hospital fifteen days after operation. A written report from his family physician six months following the transplantation of the spinal cord stated that "he has completely recovered, is working and driving a car—no sequelae."

CASE 2.—This patient, a housewife 50 years old, registered at the clinic on June 30, 1947, with a complaint of soreness in her back and inability to walk. She stated that she had been well until three and a half years before, when an aching pain developed in her back. Within three months she noticed weakness in

her legs. Rest in bed for nine months effected a cure for a year. Six months prior to registration she again noticed a gradual loss of sensation and strength in her legs. On admission she had spastic paralysis with absence of sensation below the tenth thoracic segment and increased reflexes (fig. 4). The Babinski sign was present bilaterally.

When a similar procedure was used as previously described, the granulation tissue was removed, an extradural abscess evacuated and a large bony ridge was removed in order to move the cord anteriorly. The tissue removed was considered by the pathologist to be tuberculous granulation tissue. The following day the patient noticed some improvement in her ability to move her legs, and for one week she continued to improve. At the time of her discharge, twenty-five days

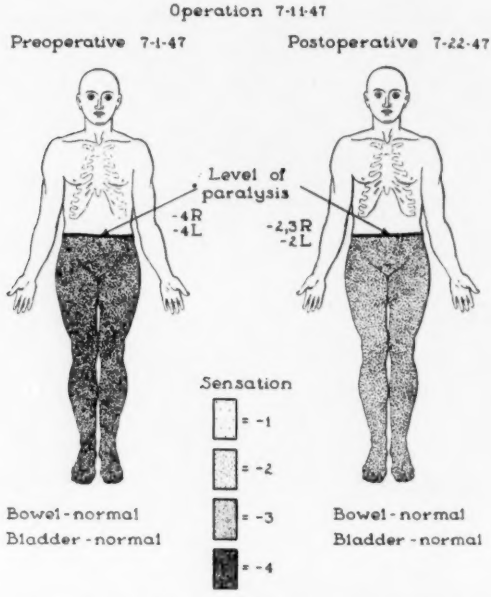

Fig. 4 (case 2).—The principal neurologic signs before operation and immediately after operation. A later follow-up revealed considerable improvement.

after operation, in spite of the use of streptomycin and rest in bed she had regressed to her former state of complete paraplegia. Because it seemed likely that her tuberculous lesion had flared up, she was advised to remain in bed for conservative treatment of the tuberculosis. Eleven months following the transplantation of her cord she wrote that strength, sensation and action were good in her legs, that she had no pain and that her general condition had improved greatly. Seventeen months after her operation roentgenologic examination of the thoracic vertebrae revealed recalcification and healing. She was then allowed to be up and was fitted with a Taylor brace.

CASE 3.—A boy, 11 years old, first registered at the clinic on Feb. 6, 1945. According to the history obtained, he had poliomyelitis at the age of 1½ or 2 years, although this was not diagnosed during the acute stage. There was also some question whether a birth injury would account for his back deformity. At the age of 6 years he was operated on for relief of flexion contracture of the right knee and afterward was able to get around well. Physical examination at the clinic showed marked kyphoscoliosis (fig. 5) with deformity of the ribs. A

Fig. 5 (case 3).—The spinal column showing marked kyphoscoliosis which had been fused with bone grafts previously (anteroposterior view).

neurologic examination showed some weakness of the right leg and a more pronounced weakness of the left leg. Sensory perception was decreased in all modalities from a level of the sixth thoracic segment. He had increased reflexes in both legs as well as bilateral Babinski signs. It was felt that he had some intrinsic disease of the cord, the nature of which was not clear. For the next two years he was seen at the clinic at various intervals, during which time orthopedic procedures, including bone graft fusion, were carried out in an effort to correct his scoliosis. His neurologic status was not changed during these

visits. He returned in June 1947, at which time he stated that he had been getting along well until April, when pain developed in both legs while he was riding a bicycle. In several days this progressed to a complete spastic paralysis of both legs. Neurologic examination (fig. 6) at this time showed marked weakness of the abdomen and both lower extremities, with increased reflexes, ankle clonus and bilateral Babinski signs. The sensory level was felt to be between the fifth and seventh thoracic segments. Since lumbar and thoracic spinal punctures were unsuccessful, radiopaque oil was injected into the cisterna magna by one of us (J. G. L.). Roentgenoscopy revealed a block (fig. 7) at the level of the fifth thoracic vertebra.

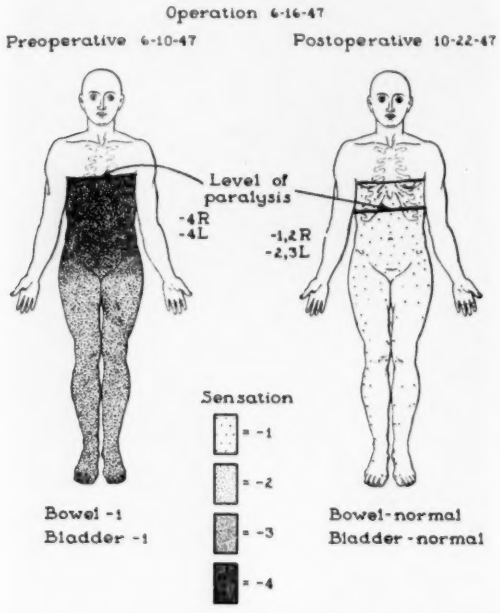

Fig. 6 (case 3).—The essential neurologic findings prior to operation and the marked improvement which was obvious four months later.

With the procedure previously described, it was found at operation that the cord was compressed at the level of the apex of the kyphos. When a portion of a bone graft previously placed along with the lamina was removed, normal pulsation of the spinal cord was resumed. A probe passed up and down the spinal canal revealed no further obstruction. There was no evidence of tuberculosis.

When the patient was reexamined two weeks later, no significant neurologic change could be detected, but on his return in October 1947, four months after operation, he could stand and his weakness was considerably less. There was no change in the sensory level, but there was some return of sensation in a patchy fashion in both lower extremities.

CASE 4.—The patient was a man, 22 years old, whose appearance and disease closely resembled that of the patient described in case 1. He registered at the clinic because of inability to walk, which had its onset about one year previously. According to the patient, he had sustained an injury at the age of 3 years which left his back and chest deformed. One year prior to registration he noticed pain in the right lower abdominal quadrant and right thigh. This lasted for about two weeks. Shortly thereafter he noticed some difficulty in ascending stairs due to weakness of his right leg, which progressed so that in three weeks he was unable to walk. This motor impairment remained stationary for the next nine months. He complained of no sensory disturbances, nor did he have any difficulty controlling his bowels or his bladder.

Fig. 7 (case 3).—Myelogram with the head up after injection of radiopaque oil showing complete block of the oil in the upper thoracic portion of the spinal canal.

Except for the injury mentioned, he had had no serious illnesses. At the age of 3 months he was closely associated with an aunt who had tuberculosis.

Examination revealed a small, thin man with marked kyphosis of the thoracic portion of the spinal column. Neurologic examination (fig. 8) showed moderate weakness of the left leg and marked weakness of the right leg. All deep reflexes were increased in the lower extremities; bilateral ankle clonus was present, and Babinski's signs were elicited bilaterally. Sensation was considered to be intact.

Except for mild anemia, laboratory studies showed nothing significant. Roentgenologic examination of the spinal column revealed pronounced thoracic kyphosis, which most probably was due to Pott's disease of the middle thoracic vertebrae.

It was felt the patient had marked compression of the cord in the thoracic region; hence exploration was advised.

One of us (J. G. L.), using the procedure previously described, transplanted the patient's spinal cord anteriorly after sufficient bone had been removed with a rongeur, chisel and cranial perforator from the posterior portion of the body of the vertebra which was displaced and was compressing the spinal cord. The abnormal tension of the spinal cord was thus relieved. A specimen of granulation tissue surrounding the spinal cord was submitted to the laboratory for smear, culture and guinea pig inoculations.

Immediately after the operation the patient's movements were extremely limited. He was capable of some slight motion in the right lower extremity and scarcely

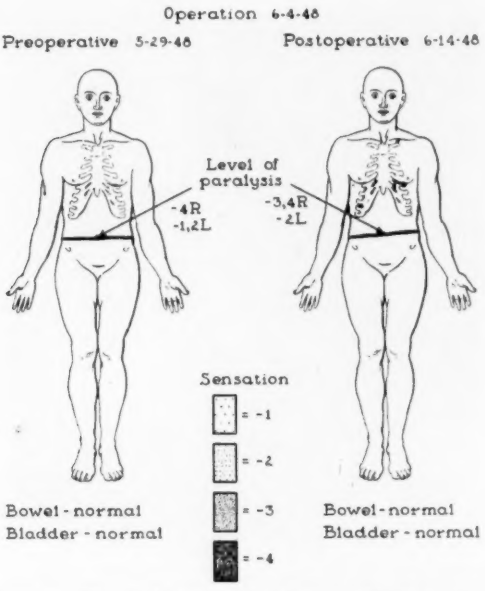

Fig. 8 (case 4).—The marked motor impairment without sensory loss before and after operation.

little more in the left. His temperature rose to 104 F., but nothing in his clinical condition seemed to indicate anything more serious than a febrile reaction to a blood transfusion. Several days later the patient was allowed out of bed, and after the lesion had been proved to be tuberculous he was treated with streptomycin. Neurologic examination ten days after operation showed almost complete paralysis of the right lower extremity and moderate weakness of the left. Signs indicative of a lesion in the pyramidal tract were present to about the same degree as before operation.

The wound was well healed in three weeks, at which time the patient was allowed to go home. Continuation of treatment with streptomycin for another three months was advised.

The next case is of interest in that no tuberculous process was present but a congenital anomaly of the thoracic portion of the spinal column was responsible for the paraplegia.

CASE 5.—This patient, a student 17 years old, registered at the clinic on Sept. 18, 1948, with the complaint of loss of function in both legs. He had apparently been well until the winter of 1947-1948, when he fell during a hockey game and shortly afterward noted that his left knee seemed to "give way" because of weakness. By June 1948, his legs were weaker, and in the next month the weakness progressed so that by August he was unable to walk without staggering. He was hospitalized elsewhere and found to have marked weakness and incoordination of both legs with increased reflexes and bilateral Babinski signs. The sensory level was at the third or fourth thoracic segment. Roentgenograms of the thoracic portion of the spinal column revealed the fifth thoracic vertebra to be a hemivertebra with the left side absent. Laminectomy was performed from the fourth to the sixth thoracic vertebra. Although the dura was seen to pulsate, the spinal cord was kinked. When the dura was opened, a catheter could readily be passed up and down the subarachnoid space. Because a tumor was not found, a bone graft was placed from the third to the sixth thoracic vertebra, inclusive. On examination after operation, complete paraplegia with the sensory level at the fifth thoracic segment was found. It was felt that postoperative edema had further damaged the already poorly functioning spinal cord. The paraplegia did not improve, but the patient did show a minimal amount of recovery of sensation within a week. (This information was furnished by the referring surgeon.)

The patient's family and past medical history were noncontributory to his present illness.

On examination at the clinic, the marked deformity of the thoracic portion of the spinal column with its convexity toward the right was obvious on inspection. No other abnormalities from a general standpoint were noted. Neurologically, the patient showed complete paraplegia and a sensory loss for all modalities below the nipple line (fig. 9). Reflexes were increased in the lower extremities; Babinski signs and ankle clonus were present bilaterally. The patient was incontinent of urine and feces. No evidence of tuberculosis or malignant disease could be found. Roentgenograms of the spinal column revealed a marked dorsal scoliosis with angulation at the level of the fifth thoracic vertebra. There were thirteen thoracic vertebrae and thirteen ribs on the right and only twelve on the left. The fifth vertebra was a hemivertebra with the left side absent. Evidence of the previous laminectomy and the bone graft were noted. Laboratory studies revealed the presence of albumin and pus in the urine but gave otherwise normal or negative results.

Inasmuch as the nature of the paralysis was felt to be indeterminate, all consultants who had seen the boy believed an exploration to be indicated.

Just prior to the exploration a lumbar puncture was performed, which revealed complete subarachnoid block. The total protein of the cerebrospinal fluid was 300 mg. per hundred cubic centimeters, and the cell count revealed 14 lymphocytes per cubic millimeter. With the patient in the face down position, one of us (J. G. L.) carried out costotransversectomy of the third, fourth and sixth ribs and corresponding vertebrae on the left side with lateral retraction of the left trapezius and rhomboid muscles and mesial retraction of the semispinalis muscles. The remaining portions of the third, fourth and sixth thoracic laminas on the left, along with the articular facets, pedicles and portions of the intervertebral disks, were removed in order to allow the angulated and compressed spinal cord to assume

a more nearly longitudinal course and also to move to the left. It thus obtained a shorter course than it could obtain in its old position, where it went over the apex of the scoliosis to the right. Likewise, it was considered that this procedure would allow the spinal cord to drop anteriorly and thus prevent its compression by the kyphotic vertebrae. The fourth and sixth thoracic nerve roots on the left were clipped with silver clips and divided because they were tense and tugged on the common dural sac. At the completion of these steps in the operation, the cord had straightened out satisfactorily, although pulsations did not go the entire extent of the operative site. The dura was thickened on the outside as though there had been some organization around it, but there was no evidence of tuberculosis. The dura was opened, and obliteration of the subarachnoid pathways due to adherence

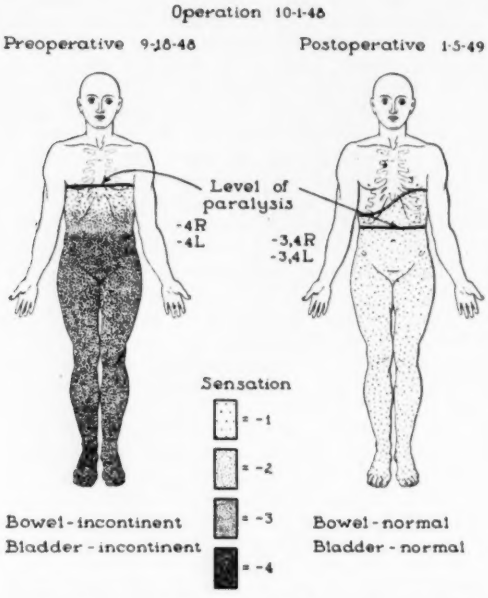

Fig. 9 (case 5).—The essential neurologic findings prior to operation and about four months after operation, at which time considerable improvement had occurred.

of the arachnoid and dura to the cord was noted. No cerebrospinal fluid was obtained on opening the dura and arachnoid; so it was left open for decompressive purposes. The previously placed bone graft was not disturbed.

The patient's postoperative course was rather uneventful. A minor infection of the urinary tract, which was easily controlled with chemotherapy, developed. The patient became afebrile by the fourth postoperative day, and the skin sutures were removed on the eleventh day. Physical therapy was given after the tenth postoperative day and in several weeks the patient's bowels and bladder were functioning properly. In six weeks he was allowed out of bed in a wheelchair with a Taylor spine brace for support. During this time repeated neurologic

examinations were made showing some slight improvement. The last examination, made approximately three months after operation, showed definite improvement in both motor strength and sensation. The patient was able to dorsiflex the toes of both feet, and, whereas previously sensation was diminished below the nipple line, he now was able readily to distinguish pain, touch and temperature in this region. His bowels and bladder were normally controlled.

COMMENT

In 3 of these cases acute paralysis developed some time prior to operation, while in 1 (case 1) surgical treatment was given soon after paraplegia developed. There is little comparison in the results.

Although it is only speculation to say that the 3 patients who had paraplegia for some time could have been relieved by prompter surgical treatment, it is significant that the patient who had paralysis of shortest duration recovered more promptly and completely after transplantation of the spinal cord. It can be pointed out also that with the advent of streptomycin one of the principal objections to exploration of a tuberculous process involving the spinal cord may be minimized.

SUMMARY

Five cases of anterior transplantation of the spinal cord are presented with the belief that this procedure has some value in the treatment of Pott's disease with associated paralysis. Likewise, it may prove useful in other conditions (cases 3 and 5) in which the pathologic process involves compression of the spinal cord by a bony ridge which interferes with normal conduction of nervous impulses.

ADDENDUM.—After this paper had been completed, our attention was called to that of Dott, N.: Skeletal Traction and Anterior Decompression in the Management of Pott's Paraplegia, Edinburgh M. J. **54**:620, 1947.

EPITHELIOMA OF THE LOWER LIP

Evaluation of Dissection of Cervical Lymph Nodes

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THERE is considerable diversity of opinion regarding the treatment of the region of the cervical lymph nodes in the presence of labial and intraoral malignant lesions. As Wilson [1] pointed out, the lymphatic spread of cancer may vary according to the primary site and therefore the results should be studied in terms of the origin of the metastatic lesions. In this paper we shall present only the results of treatment of the neck in squamous cell epithelioma of the lower lip.

The trend in the treatment of cervical nodes, as Duffy [2] has pointed out, has progressed from radical surgical procedures, pioneered by Kocher, Cheattle, Bloodgood and Crile, through extensive use of radiation at some centers to a consideration of the two methods separately or in combination.

It is felt that metastatic lesions develop by lymphatic emboli rather than by direct extension.[3] Therefore, the treatment of the secondary lesion can be considered to be separate from that of the primary lesion and the intervening tissue does not have to be removed.

Kennedy [4] has pointed out that there has been no improvement in the death rate from carcinoma of the lip in the United States since the advent of radiation treatment of cervical nodes. There have been no reported five year cures in the literature in the past fifteen years

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Dr. Judd is from the division of surgery of the Mayo Clinic.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Wilson, H.: Results of the Treatment of Metastatic Carcinoma in the Cervical Lymph Nodes: A Collective Review of the Recent Literature, Internat. Abstr. Surg. **75**:403-413 (Nov.) 1942.

2. Duffy, J. J.: Cervical Lymph Nodes in Intraoral Carcinoma: Surgery or Irradiation? Am. J. Roentgenol. **39**:767-777 (May) 1938.

3. Quick, D.: Management of Cancer of the Mouth and the Cervical Lymphatics, Am. J. Roentgenol. **31**:366-377 (March) 1934.

4. Kennedy, R. H.: The Management of Lymph Nodes in the Neck—Metastatic from Carcinoma of the Mouth, Ann. Surg. **114**:813-819 (Nov.) 1941.

from the use of external radiation to the cervical nodes when metastasis has been established by biopsy.[5] Hayes Martin[6] has reported a five year survival rate of 51.1 per cent when interstitial irradiation is used.

It is the consensus of most authors that when the cervical nodes are involved and considered operable surgical intervention is always indicated. Operability may be established by Duffy's[2] indication. In cases of inoperable cervical nodes the patient must be given whatever palliative treatment may give him symptomatic relief.

The controversial question remains then: "What treatment should be given the patient in whom the cervical nodes are not palpable or are palpable but are considered benign?" One school of thought is that of expectancy—to "wait and see." This attitude has been supported by Martin,[6] Duffy,[2] Quick,[3] Wile and Hand,[7] Howes and LaRosa,[8] Sugarbaker[9] and others; in accord with it, surgical treatment of the neck is not undertaken until cervical nodes are palpable and considered clinically positive for metastases. The other school of thought supports the so-called prophylactic neck dissection, in which surgical treatment of the neck of a limited degree is carried out in selected cases in which cervical nodes are or are not palpable and are considered clinically negative for metastasis. Blair, Brown and Byars,[10] Kennedy,[4] Figi,[11] Dixon,[12] Wangensteen and Randall,[13] Mayne,[14] and Brown and McDowell[5] have supported this view.

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5. Brown, J. B., and McDowell, F.: Treatment of Metastatic Carcinoma of the Neck, Tr. South. S. A. **55**:254-266, 1944.

6. Martin, H.: The Treatment of Cervical Metastatic Cancer, Ann. Surg. **114**:972-985 (Dec.) 1941.

7. Wile, U. J., and Hand, E. A.: Cancer of the Lip: Results of Therapy in Four Hundred and Twenty-Five Cases Followed from One to Ten Years, J. A. M. A. **108**:374-382 (Jan. 30) 1937.

8. Howes, W. E., and LaRosa, F. J.: Carcinoma of the Lower Lip: Interval Statistical Survey of the End-Results in All Cases Treated at the Brooklyn Cancer Institute, 1930 to 1939 Inclusive, Am. J. Roentgenol. **47**:39-49 (Jan.) 1942.

9. Sugarbaker, E. D.: The Surgical Problem of Cancer in Lymph Nodes, Surgery **18**:608-619 (Nov.) 1945.

10. Blair, V. P.; Brown, J. B., and Byars, L. T.: Our Responsibility Toward Oral Cancer, Ann. Surg. **106**:568-576 (Oct.) 1937.

11. Figi, F. A.: Epithelioma of the Lower Lip, Surg., Gynec. & Obst. **59**:810-819 (Nov.) 1934.

12. Dixon, C. F.: Submental and Bilateral Submaxillary Dissection: Colostomy as First Stage in Operation for Carcinoma of Upper Part of Sigmoid; Exteriorization Operation for Sigmoidal Polyp, S. Clin. North America **15**:1303-1307 (Oct.) 1935.

13. Wangensteen, O. H., and Randall, O. S.: Treatment and Results in Carcinoma of Lip: Report of a Hundred and Thirty Cases, Am. J. Roentgenol. **30**:75-81 (July) 1933.

14. Mayne, W.: Cancer of the Mouth: Its Present Day Treatment, Am. J. M. Sc. **210**:548-554 (Oct.) 1945.

Hayes Martin [6] pointed out that in only 4 (3 per cent) of 128 cases of cancer of the lip did cervical metastasis later develop and cited this low incidence of cervical metastasis as not outweighing the risk of prophylactic surgical treatment. Duffy [2] strongly supported this view. Others have reported a higher incidence of metastasis in patients in whom prophylactic neck dissections have been performed. Kennedy,[4] in a series of 64 cases of carcinoma of the lower lip, found metastasis in 9 instances (14 per cent). He stated that cervical metastases will occur in 20 to 25 per cent of such cases. Simmons and Daland [15] reported similar findings in 25 per cent.

Blair, Brown and Byars [10] expressed the belief that neither clinical examination nor the routine histologic examination of removed lymph nodes disproves the presence of carcinoma cells, and they added that "only the passage of time can disprove their presence." Kennedy emphasized that simply because the pathologist in a routine examination fails to find carcinoma in removed cervical nodes one may not always assume that no metastases are present.

Morrow [16] expressed the opinion that successful treatment depends on keeping ahead of the disease and that this best can be done by routine neck dissection, whether nodes are palpable or not. Taylor and Nathanson [17] emphasized that an adequate follow-up course is the determining factor in the decision for or against prophylactic neck dissection in many cases. There is no experimental evidence to support Quick's view that the normal nodes tend to act as a barrier to carcinoma cells and in some instances actually destroy a number of small metastases. In the opinion of Wile and Hand,[7] Moreland [18] and Martin,[19] prophylactic irradiation of the neck is unnecessary, since there is no real proof that small doses will destroy cancer. Slaughter [20] added that the light doses used accomplish nothing except to confuse the situation. Wile and Hand,[7] in a study of 425 cases of carcinoma of

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15. Simmons, C. C., and Daland, E. M.: The Results of Operations for Cancer of the Lip at the Massachusetts General Hospital from 1909 to 1919, Surg., Gynec. & Obst. **35**:766-771 (Dec.) 1922.

16. Morrow, A. S.: Cancer of the Tongue: A Report of One Hundred and Eighty-Seven Cases, With an Analysis of Ninety-Eight Treated Principally by Surgery at the New York Skin and Cancer Hospital Between 1917 and 1935, Ann. Surg. **105**:418-441 (March) 1937.

17. Taylor, G. W., and Nathanson, I. T.: Evaluation of Neck Dissection in Carcinoma of the Lip, Surg., Gynec. & Obst. **69**:484-492 (Oct.) 1939.

18. Moreland, R. B.: The Treatment of Metastatic Carcinoma of the Neck, Secondary to Carcinoma of the Lip, J. A. M. A. **110**:1084-1087 (April 2) 1938.

19. Martin, H. E.: Treatment of Cancer of the Lip, Am. J. Surg. **30**:215-226 (Nov.) 1935.

20. Slaughter, D. P.: Neck Dissections: Indications and Technics, S. Clin. North America **26**:102-115 (Feb.) 1946.

the lip, reported 40 per cent five year cures from suprahyoid dissections in cases in which there was evidence of carcinoma in the cervical nodes.

Newell [21] reported 390 cases of carcinoma of the lip and reported 80.9 per cent five year cures by excision of the primary lesion only in cases with no metastases clinically, 85.3 per cent by excision of the tumor and neck dissection in cases without metastases and 22.5 per cent five year cures in cases in which radical neck dissection was done because of metastases. Kennedy [4] reported a 26 per cent five year cure rate following neck dissection for proved cervical metastases. Wile and Hand [7] reported a 40 per cent five year survival rate in patients with clinical metastases after neck dissection. Figi [11] reported a 39 per cent five year survival rate. Hayes Martin [6] reported 5 cases of five year survival in 21 cases of cervical metastases from lesions of the lower lip treated by neck dissection. Slaughter's recent figure for carcinoma of the lip after neck dissection is 33 per cent five year cures.[20] His over-all figure is 70 per cent five year survival rate. Taylor [22] reported 58 per cent cures after neck dissection in patients with involved nodes secondary to carcinoma of the lip. The interval was not stated.

PRESENT STUDY

From Jan. 1, 1930 through Dec. 31, 1939 802 patients with squamous cell epithelioma of the lower lip were seen at the Mayo Clinic. A review of the cases was undertaken primarily to determine survival rates according to grade of malignancy and type of treatment to the neck. In 28 of the cases, when the patients were first seen at the clinic the lesions were considered inoperable and hopeless as to cure from any form of treatment. Treatment in these cases was palliative. The series which is evaluated in this paper is composed of the 774 nonpalliative cases, which represent 96.5 per cent of the total number of cases.

THE LESION OF THE LIP

Because Figi [11] earlier had noted a difference in behavior between the epitheliomas of the lip which had previously been treated and those which had not received treatment, this series was divided into a primary group—those that had not received previous treatment to the lip—and a secondary group—those that had received previous treatment to the lip. Four hundred and fifty cases (58.1 per cent) were in the primary group and 324 (41.9 per cent) in the secondary group. Of the latter group, in about a third previous surgical treatment (including cautery) had been given, in a third caustics and escharotics had been used and in a third radiation therapy had been given.

21. Newell, E. T., Jr.: Carcinoma of the Lip: Clinical and Pathologic Study of Three Hundred and Ninety Cases, With Report of Five Year Cures, Arch. Surg. **38**:1014-1029 (June) 1939.

22. Taylor, G. W.: Evaluation of Regional Lymph-Node Dissection in the Treatment of Carcinoma, New England J. Med. **226**:367-371 (March 5) 1942.

Lesions of the lower lip were all graded according to the Broders method (grade 1 being the least and grade 4 the most malignant). The growths varied as to their activity, but most of them were of low or moderate activity. Forty-two and four-tenths per cent were grade 1; 39.4 per cent were grade 2; 12.1 per cent were grade 3, and 1.8 per cent were grade 4; in 4.3 per cent the grade was not stated.

Epithelioma of the lower lip is still predominantly a disease of males. Of the 774 patients, 763 (98.6 per cent) were males and 11 (1.4 per cent) were females. This corresponds closely to the sex incidence as previously reported in the literature. The ages of the patients varied from 13 to 87 years, with an average age of 56.7 years. Eleven per cent of the patients were less than 40 years of age, and 30.5 per cent were less than 50 years of age. The age incidence is shown in table 1.

TABLE 1.—*Age Incidence of Epithelioma of the Lower Lip*

	Patients	
Age, Years	Number	Percentage
13-19	1	0.1
20-29	12	1.6
30-39	73	9.4
40-49	150	19.4
50-59	235	30.4
60-69	179	23.1
70-79	101	13.0
80-87	23	3.0

The average duration of symptoms for the primary group was 18.9 months, for the secondary group 30.0 months and for the total series 23.7 months. The size of the lesion in the primary group was somewhat smaller than in the secondary group. The average size in the former was 1.5 cm. in diameter, whereas in the latter it was more than 2 cm. in diameter. Approximately 40 per cent of the lesions were on the right side of the lower lip, 40 per cent on the left and 20 per cent in the midportion. In 18 (2.3 per cent) of the cases a new lesion of the lower lip developed after the first epithelioma had been controlled. Forty-two patients (5.4 per cent) had multiple lesions on the lower lip when first treated. In 33 cases (4.3 per cent) recurrent lesions developed during the follow-up period, 24 (72.7 per cent) of these cases being in the secondary group. Incidentally, in 65 cases (8.4 per cent) malignant lesions other than of the lower lip are known to have developed during the follow-up period.

Treatment of the primary lesion of the lower lip at the Mayo Clinic is chiefly by excision with a scalpel, using either the V excision or the lip shave technic or a combination of the two with immediate or delayed plastic reconstruction of the lower lip when this is indicated. Accord-

ingly, 738 (95.3 per cent) received surgical treatment for the primary lesion of the lip. Fourteen patients (1.8 per cent) received radiation therapy, and in 22 cases (2.9 per cent) no treatment was indicated because previous treatment of the lip had been satisfactory.

The risk of surgical treatment of the primary lesion of the lip is very slight. In the 738 cases there were 2 deaths, representing a hospital mortality rate of 0.27 per cent. One patient died on the sixth postoperative day of pulmonary embolism, while the other, a patient 77 years of age with old pulmonary tuberculosis, died on the nineteenth day after radon seeds had been implanted in the lesion of the lip.

CERVICAL DISSECTION

The hospital mortality rate for those patients receiving surgical treatment to the cervical nodes is correspondingly low. In the 357 cases in which bilateral suprahyoid neck dissection or bilateral suprahyoid

TABLE 2.—*Accuracy of Diagnosing Palpable Cervical Nodes in Epithelioma of the Lower Lip*

	Clinically Negative				Clinically Positive				Total			
Group	Total	Proved	Per Cent Correct	Per Cent Erroneous	Total	Proved	Per Cent Correct	Per Cent Erroneous	Clinically Diagnosed	Proved	Per Cent Correct	Per Cent Erroneous
Primary	25	23	92.0	8.0	12	7	58.3	41.7	37	30	81.1	18.9
Secondary	18	18	100.0	0	63	41	65.1	34.9	81	59	72.8	27.2
Both	43	41	95.3	4.7	75	48	64.0	36.0	118	89	75.4	24.6

neck dissection with a unilateral block dissection was performed there was 1 death, a mortality rate of only 0.28 per cent. This patient had clinically involved cervical nodes which made surgical treatment imperative. He was a poor surgical risk because of questioned pulmonary tuberculosis. He died on the fourteenth postoperative day of bronchopneumonia. There were no deaths in cases in which operations were done as prophylactic neck dissections. Hayes Martin [6] reported a neck dissection mortality rate of 2.4 per cent. Figi [11] has previously reported a mortality rate of 0.18 per cent from the Mayo Clinic.

Thirty-one per cent of the patients had palpable cervical nodes, half of which were said to be small. In the primary group 20.7 per cent had nodes which were palpable, whereas in the secondary group, the nodes of 45 per cent were palpable.

ERROR IN DIAGNOSIS

The clinical diagnosis of metastatic involvement of cervical lymph nodes is not infallible. In the 118 cases in which the cervical nodes were definitely stated to be clinically negative or clinically positive, an

error of 24.6 per cent was proved after the tissue was removed and examined in the pathologic laboratory. This figure is broken down in table 2. Fortunately, the greatest error was in calling negative nodes positive for metastases. Duffy [23] stated that this error is between 15 and 35 per cent. When palpable nodes not stated to be either negative or positive are assumed to be negative, the clinical error in diagnosis is 20.1 per cent. As noted in table 3, of the total group 299 patients were stated to have clinically negative cervical nodes, palpable nodes considered negative or nonpalpable nodes. Of this number, 21 patients (7.0 per cent) proved to have metastases. In other words, 7 of 100 patients had metastases to the cervical nodes which were not diagnosed clinically. Jorstad,[24] who has stated that he prefers not to do a routine neck dissection but to wait for palpable nodes, found 66 per cent positive for metastases when neck dissection was done.

TABLE 3.—*Over-All Error in Clinical Diagnosis of Cervical Metastases in Epithelioma of the Lower Lip*

Nodes	Number	Negative	Positive	Percentage Positive
Clinically negative	43	41	2	4.7
Palpable, considered negative	90	77	13	14.4
Nonpalpable	166	160	6	3.6
Total	299	278	21	7.0

SURVIVAL RATES

Table 4 shows the survival rates according to grade of malignancy for traced patients for the five year and ten year intervals. It is interesting to note, as expected, that the survival rates are directly related to the activity of the lesion as expressed in grade; for example, the lower the grade of the lesion the better the survival rate. There is also a definite variation between the primary and the secondary groups. Those patients who had not received previous treatment to the lesion of the lip have a 9 per cent better survival rate in the five year period than the group that had received some previous treatment. In the ten year period the rate for the primary group is 10.2 per cent better than that for the secondary group. The five year survival rate for the total series is 79.3 per cent and the ten year rate is 61.8 per cent.

The five year and ten year survival rates according to type of treatment to the neck are shown in tables 5 and 6. The patients not receiving

23. Duffy, J. J.: Treatment of Cervical Nodes in Intra-Oral Cancer, Surg., Gynec. & Obst. **71**:664-671 (Nov.) 1940.

24. Jorstad, L. H.: Diagnosis, Treatment and Prognosis of Carcinoma of Buccal Mucosa, South. M. J. **35**:970-973 (Nov.) 1942.

TABLE 4.—*Survival Rate of Epithelioma of the Lower Lip According to Grade of Malignancy*

Grade of Malignancy of Labial Lesion	Patients *		Lived Five Years or More After Treatment		Patients *		Lived Ten Years or More After Treatment	
	Total	Traced	Number	Percentage of Traced Patients	Total	Traced	Number	Percentage of Traced Patients
Primary group								
Grade 1.....	234	197	170	86.3	194	132	93	70.5
Grade 2.....	169	150	125	83.3	151	123	82	66.7
Grade 3.....	39	34	24	70.6	37	27	16	59.3
Grade 4.....	5	5	3	60.0	5	5	1	20.0
Grade unstated	3	3	1	33.3	3	3	0	0
Total.....	450	389	323	83.0	390	290	192	66.2
Secondary group								
Grade 1.....	94	80	67	83.7	85	62	42	67.7
Grade 2.....	136	115	90	78.3	120	96	57	60.0
Grade 3.....	55	46	30	65.2	49	34	15	44.1
Grade 4.....	9	9	5	55.6	9	8	4	50.0
Grade unstated	30	27	13	48.1	24	19	4	21.1
Total.....	324	277	205	74.0	287	218	122	56.0
Total series.....	774	666	528	79.3	677	508	314	61.8

* Inquiry as of Jan. 1, 1949. All patients are included in the five year group; the ten year group includes those patients treated in 1938 or earlier.

TABLE 5.—*Five Year Survival Rates of Epithelioma of the Lower Lip According to Type of Treatment to the Neck*

Type of Treatment	Patients Traced *	Lived Five Years or More After Treatment		Grades 1 and 2			Grades 3 and 4		
		Number	Percentage	Patients Traced *	Lived Five Years or More After Treatment		Patients Traced *	Lived Five Years or More After Treatment	
					Number	Percentage		Number	Percentage
Primary group									
No treatment.....	188	157	83.5	182	154	84.6	5	2	40.0
Prophylactic suprahyoid dissection	131	112	85.5	105	93	88.5	26	19	73.1
Prophylactic irradiation.....	62	51	82.3	55	46	83.6	6	5	83.3
Suprahyoid + block dissection	7	3	42.9	5	2	40.0	2	1	50.0
Irradiation	1	0	0	0	0	0	0	0	0
Total	389	323	83.0	347	295	85.0	39	27	69.2
Secondary group									
No treatment.....	68	56	82.4	60	51	85.0	4	3	75.0
Prophylactic suprahyoid dissection	147	120	81.6	106	91	85.8	31	24	77.4
Prophylactic irradiation.....	20	11	55.0	15	9	60.0	4	2	50.0
Suprahyoid + block dissection	37	17	45.9	13	6	46.1	13	6	46.2
Irradiation	5	1	20.0	1	0	0	3	0	0
Total	277	205	74.0	195	157	80.5	55	35	63.6
Total series.....	666	528	79.3	542	452	82.8	94	62	66.0

* Inquiry as of Jan. 1, 1949. There were 30 cases in which the grade of malignancy was not stated.

treatment to the neck had small lesions of short duration, low cellular activity as a rule and little or no inflammation of the lip. In this group it is felt that the treatment to the primary lesion adequately controls the disease. Included in the group with a "prophylactic suprahyoid dissection" are those who received bilateral resection of submaxillary and submental nodes with or without the removal of the deep upper cervical nodes. In patients receiving prophylactic irradiation preoperatively or postoperatively to the labial lesion, prophylactic neck dissection was not felt to be indicated or the patients refused neck

TABLE 6.—*Ten Year Survival Rates of Epithelioma of the Lower Lip According to Type of Treatment to the Neck*

				Grades 1 and 2			Grades 3 and 4		
		Lived Ten Years or More After Treatment			Lived Ten Years or More After Treatment			Lived Ten Years or More After Treatment	
Type of Treatment	Patients Traced *	Number	Percentage	Patients Traced *	Number	Percentage	Patients Traced *	Number	Percentage
Primary group									
No treatment	133	88	66.2	129	88	68.2	3	0	0
Prophylactic suprahyoid dissection	108	78	72.2	85	64	75.3	23	14	60.9
Prophylactic irradiation	43	24	55.8	37	22	59.5	5	2	40.0
Suprahyoid and block dissection	5	2	40.0	4	1	25.0	1	1	100.0
Irradiation	1	0	0	...	..	....	..	..	....
Total	290	192	66.2	255	175	68.6	32	17	53.1
Secondary group									
No treatment	48	28	58.3	44	27	61.4	2	1	50.0
Prophylactic suprahyoid dissection	121	80	66.1	89	64	71.9	22	12	54.5
Prophylactic irradiation	17	6	35.3	12	4	33.3	4	2	50.0
Suprahyoid and block dissection	28	8	28.6	11	4	36.4	11	4	36.4
Irradiation	4	0	0	1	0	0	3	0	0
Total	218	122	56.0	157	99	63.1	42	19	45.2
Total series	508	314	61.8	412	274	66.5	74	36	48.6

* Inquiry as of Jan. 1, 1949. Included here are only those patients treated in 1938 or earlier. There were 22 cases in which grade of malignancy was not stated.

dissection. This group also includes those patients requesting roentgen treatment. We do not feel that the amount of external radiation given in these cases is of any therapeutic value. The group having a suprahyoid plus a unilateral block dissection all had metastases. In these cases the sternocleidomastoid muscle and the internal jugular vein were sacrificed on one side. The number receiving radiation alone is negligible.

The patients who had a prophylactic suprahyoid dissection have a better survival rate in the five year period than the group not receiving that treatment. These survival rates are substantially better than the rates for those receiving prophylactic radiation. Thirty-four patients, mostly in this group, were advised to have a prophylactic suprahyoid dissection but refused. In the ten year period patients in the primary

group having a suprahyoid dissection had a 6.0 per cent better chance of living than those having no such treatment and 16.4 per cent better chance of living than those receiving prophylactic radiation. This held true for the secondary group also. It is interesting to note that the survival rates in the secondary group are lower than in the primary group when determined according to type of treatment to the neck, as they also were when classified by grade of malignancy.

In 74 cases nodal metastasis was established by microscopic examination. This represents 9.6 per cent of the total cases. Twenty-one and six-tenths per cent of these were in the primary group and 78.4 per cent were in the secondary group. In 4 cases the tumor was of grade 1, in 22 of grade 2, in 19 of grade 3, in 9 of grade 4; in 20 the grade was not stated.

TABLE 7.—*Survival Rates of Patients with Epithelioma of the Lower Lip and Cervical Metastases*

	Patients *		Lived Five Years or More After Treatment		Patients *		Lived Ten Years or More After Treatment	
	Total	Traced	Number	Percentage of Traced Patients	Total	Traced	Number	Percentage of Traced Patients
Primary	16	16	7	43.8	14	14	5	35.7
Secondary	58	55	26	47.3	50	49	15	30.6
Total	74	71	33	46.5	64	63	20	31.7

* Inquiry as of Jan. 1, 1949. All patients are included in the five year group; the ten year group includes those patients treated in 1938 or earlier.

The survival rates of patients with proved metastatic cancer are found in table 7. The five year rate of survival is 46.5 per cent, and the ten year rate is 31.7 per cent for these cases.

SUMMARY

For patients who have an epithelioma of the lower lip with clinical evidence of metastasis to the cervical lymph nodes, surgical intervention by bilateral removal of the submaxillary salivary glands and lymph nodes and the submental nodes and unilateral dissection of the upper deep cervical nodes on the involved side is indicated. Block dissection of the anterior triangle of the neck with removal of the sternocleidomastoid muscle and the internal jugular vein is carried out when the upper deep jugular nodes are involved or the suprahyoid mass is large.

Interstitial radiation is recommended when the nodes are considered inoperable or the lesion is grade 4.

Prophylactic irradiation is considered a placebo.

For patients without clinical evidence of cervical metastatic lesions but with palpable nodes considered negative or without palpable nodes, a prophylactic suprahyoid node dissection is recommended under certain conditions.

If the labial lesion is grade 1, neck dissection is not advised unless the lesion is of long duration, large, infected, with considerable inflammatory reaction about it and probably of secondary character.

The majority of metastatic lesions are grades 2 and 3; therefore prophylactic dissection of nodes is recommended in all these cases, except for a few patients whose age or general condition does not permit major surgical intervention. In an occasional case in which the grade 2 primary lesion is treated early and the lesion is small, neck dissection might be omitted.

In early grade 4 lesions prophylactic neck dissection may be done, but usually there has already been metastasis and the lesions frequently are inoperable.

CONCLUSIONS

The following factors support prophylactic dissection of cervical nodes: the high clinical error in diagnosis of metastasis to the neck; the opportunity for removal of early metastatic lesions which develop in approximately 10 per cent of epitheliomas of the lower lip; the prevention of metastasis by blocking off the lymphatics by surgical removal; the low mortality rate of the suprahyoid dissection; a high survival rate of patients so treated, and the impossibility of adequate follow-up examination in nonresident patients.

NONOBSTRUCTIVE LATERAL PORTAL VEIN–VENA CAVA ANASTOMOSIS

A Clinical Application of the Smith Freeman Clamp

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AND
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THE APPLICATION of advancing methods of venous anastomosis to the problem of portal hypertension has demonstrated the value of surgical treatment in diminishing the dangers of hemorrhage secondary to this condition. Blakemore,[1] Whipple [2] and Linton [3] have explored the feasibility and value of a variety of methods and sites of the production of venous shunts between the portal system and the vena cava. Although Linton has reported apparent success in 2 cases, utilizing anastomosis between the superior mesenteric vein and the vena cava in 1 and between the inferior mesenteric vein and the left ovarian vein in the other, the majority of anastomoses have been splenorenal or from the portal vein to the vena cava. The operation most frequently reported has been anastomosis of the splenic vein to the left renal vein, end to side, after splenectomy. Less often an end to side anastomosis between the portal vein and the inferior vena cava has been accomplished. In 1 case Blakemore [1b] has done a side to side portal vein–vena cava shunt.

It would seem that the direct shunt between the portal vein and the vena cava would be more effective in reducing portal pressures when its accomplishment is not prevented by changes within or about the portal vein. However, the disadvantages that the portal vein is completely obstructed during the anastomosis and that the liver is deprived of portal flow by the shunt are considerable.

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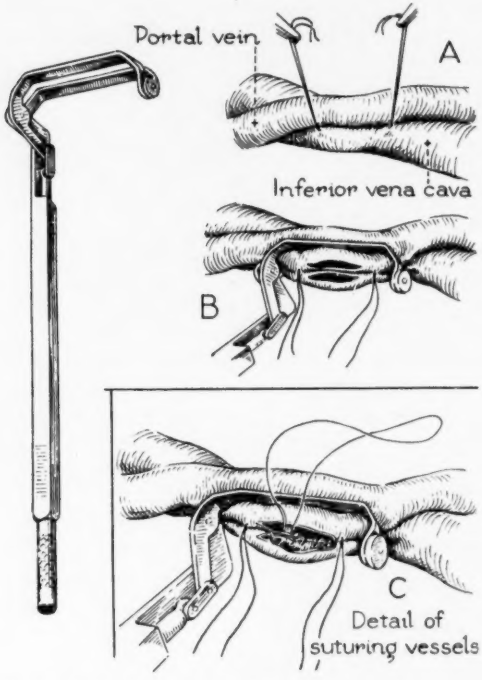
1. (*a*) Blakemore, A. H.: Surg., Gynec. & Obst. **85**:645, 1947; (*b*) Ann. Surg. **128**:825, 1948.

2. Whipple, A. O.: Ann. Surg. **122**:449, 1945.

3. Linton, R. R.; Hardy, I. B., Jr., and Volwiler, W.: Surg., Gynec. & Obst. **87**:129, 1948.

We have sought to overcome these disadvantages of direct anastomosis through the use of a new clamp devised by Smith Freeman.[4] This clamp, which was developed for Eck fistula studies in experimental animals, provides a means by which a side to side shunt between portal vein and vena cava may be made without obstructing either. Some of the difficulty encountered because of the plexus of veins in the hepatoduodenal ligament may be avoided because only



Construction of a side to side portal vein–vena cava anastomosis with use of the Freeman clamp (shown at the left). *A*, holding suture to mark the site of anastomosis; *B*, clamp in place and incisions made; *C*, placement of simple continuous suture.

the dorsal surface of the portal vein need be exposed. The line of anastomosis is selected where the two veins are in closest relationship and is demarcated by holding sutures at each end passed through all coats of both vessels and tied (figure, *A*). By careful traction on the stay sutures and compression of the vessels, the clamp is passed

4. Freeman, S.: Surg., Gynec. & Obst. **87**:735, 1948.

down over the area of proposed anastomosis and tightly closed. The adjacent folds of vein are then opened longitudinally within the stay sutures and slightly medial to the apex of the fold (figure, *B*). The clamp, in its present form, does not provide room for an everting suture, and for this reason a simple continuous suture has been used (figure, *C*).

We have used this method clinically in the following case, with satisfactory results.

W. S., a 40 year old white male cab driver, was first admitted to the vascular surgical service of the Veterans Administration Hospital, Hines, Ill., in August 1948, because of gastrointestinal hemorrhage. Since 1940 attacks of weakness associated with tarry stools and hematemesis had occurred with increasing frequency and duration. In 1946 a splenectomy was done. The hemorrhages diminished in frequency for six months following splenectomy but returned to their preoperative severe degree. Laboratory examination on admission demonstrated a severe anemia, normal prothrombin time, normal excretion of sulfobromophthalein sodium, normal protein concentration and distribution and negative cephalin flocculation test. An attempt was made to sclerose the large esophageal varices which were seen at endoscopy, but this served only to increase the bleeding. After suitable preparation with blood transfusion, the patient was operated on on Sept. 16, 1948. Through a transverse subcostal incision, the duodenum was reflected medially, exposing the hepatoduodenal ligament and the vena cava. The portal vein was surrounded by a network of thin-walled veins which made its exposure difficult. The fact that only the dorsal surface needed to be exposed lightened the labor considerably. Tension in the portal vein was found to be 310 mm. of water. Anastomosis, 1 cm. in length, was accomplished with use of the Freeman clamp without event. The portal vein tension was then measured and found to be 400 mm. of water. There was no fluctuation of the arterial blood pressure in this interval. The patient recovered rapidly from his operation and was allowed early ambulation. The stools became negative for blood on the third postoperative day. The patient gained 20 pounds (9.1 Kg.) in weight in eight weeks following operation. During the ninth week he had a single tarry stool each day for three consecutive days but experienced no other symptoms. He did not report for examination at that time. Five months postoperatively his weight gain had continued, blood counts were normal and there had been no further evidence of bleeding. The biopsy specimen from the liver, taken at the time of the anastomosis, showed a marked increase in fibrous tissue with extensive areas of regeneration.

The production of an anastomosis between the portal vein and the vena cava, in those cases in which conditions do not prevent its use, has certain advantages over the less direct splenorenal anastomosis. A greater volume of blood flow can be obtained, depending only on the length of the anastomosis which is made. Avoidance of obstruction of the veins during the operation, particularly of the portal vein, is a theoretic advantage in that it may reduce the incidence of postoperative mesenteric thrombosis. The advantage that accrues from the use of a clamp of the design described is increased by the fact that the portal vein is only partially exposed.

The disadvantages of the method are that an everting mattress suture cannot be accomplished in the present clamp and that the surgeon is left without safety devices if mechanical failure should occur in the clamp. Slipping of the instrument has not been a factor, and the superior construction of the one now in use makes breakage or stripping of threads a most unlikely danger. The obvious changes which will permit the placing of a mattress suture have already been made, but the instrument of new design has not, at this time, been tested.

CONCLUSIONS

1. There are certain advantages inherent in a side to side portal vein–vena cava anastomosis.

2. A method for producing such an anastomosis without obstruction during the operation, previously described in animal experimentation by Freeman, has been used successfully in 1 clinical case.

STERILITY AND ENDOMETRIOSIS

LEON S. McGOOGAN, M.D.
OMAHA

STERILITY is a common symptom of endometriosis. Various authors [1] have stated, as shown in table 1, that 20 to 66 per cent of the patients with endometriosis have a history of sterility. Pregnancy can occur in the presence of endometriosis, but the incidence is low.

Why are the majority of women who have endometriosis sterile? Witherspoon [2] stated that "the high frequency of sterility is due to the presence of the multiple follicular cysts of the ovaries in the absence of ovulation and subsequent formation of corpora lutea." This theory parallels that proposed as to the etiology of sterility in polycystic ovaries. This theory is not tenable for all cases, as the premenstrual phase changes characteristic of corpus luteum effect of endometrial transplants and corpora lutea have been demonstrated at operation, or in the removed ovaries. With or without the formation of a corpus luteum all cases of endometriosis of the ovaries have in common a disease process which develops in or on normal ovarian tissue. It must alter the normal blood flow and the normal intracapsular tension of the tissues of the ovary. With the recurring menstruation of the ectopic endometrium there would be produced and contained within the ovarian structures a normal or pseudonormal menstruum. There is a possibility that this menstruum or its subsequent degenerative products contain substances which might be reabsorbed by the tissues of the body and prevent the formation of an ovum, or of one incapable of being fertilized, or if fertilized, of being unable to implant itself on suitable endometrium.

From the Department of Obstetrics and Gynecology, University of Nebraska College of Medicine.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. (*a*) Abell, I., Jr.: Kentucky M. J. **44**:339, 1936. (*b*) Counseller, V. S.: Am. J. Obst. & Gynec. **37**:788, 1939; ibid. **36**:877, 1938. (*c*) Fallon, J.; Brosman, J. T., and Moran, W. G.: New England J. Med. **235**:669, 1946. (*d*) Haydan, G. B.: Am. J. Obst. & Gynec. **43**:704, 1942. (*e*) Keene, F. E., and Kimbrough, R. A., Jr.: Endometriosis: Review Based on Study of One Hundred and Eighteen Cases, J. A. M. A. **95**:1164 (Oct. 18) 1930. (*f*) Smith, V. S.: Am. J. Obst. & Gynec. **17**:806, 1929. (*g*) Turunen, A.: Acta obst. et gynec. Scandinav. **19**:477, 1939.

2. Witherspoon, J. T.: Clinical Pathological Gynecology, Philadelphia, Lea & Febiger, 1939, p. 234.

Smith and Smith [3] have shown that the normal menstrual flow contains substances toxic to the experimental animal. Would it be too much to postulate that some substance produced by the ectopic endometrium could be toxic to the ovum?

Since endometriosis is a cause of sterility, it would reasonably follow that the removal of the ectopic endometrium and its by-products would cure the sterility.

Curtis [4] states that "few patients with extensive endometriomatous lesions become pregnant after conservative surgery, and even after satisfactory operation these patients tend to remain permanently sterile."

TABLE 1.—*Reported Incidence of Sterility Among Patients with Endometriosis*

Author	%
Abell [1a]	50
Counseller [1b]	32
Fallon [1c]	66
Haydan [1d]	53
Keene & Kimbrough [1e]	40.9
Smith [1f]	20.6
Turunen [1g]	45

TABLE 2.—*Reported Incidence of Pregnancy Following Conservative Operation*

Author	No. Cases	Pregnancy, No.	%
Whorton [5d]	4	3	75
Counseller [1b]	55	7	12.7
Cattell [5a]	21	3	14.2
Payne [5b]	73	13	17.8
Keene & Kimbrough [1e]	14	4	28
Turunen [1g]	84	26	31.7
Schmitz & Towne [5c]	47	11	23.6
Total	298	67	22.4

Various authors [5] have stated, as is shown in table 2, that 13 to 75 per cent of the patients operated on become pregnant.

A careful analysis of these reports reveals that the following factors have not always been taken into consideration: (1) type of operation, (2) fertility of the husband, (3) desire for pregnancy, and (4) presence of other factors which of themselves might be factors in producing sterility.

3. Smith, O. W., and Smith, G. V.: Proc. Soc. Exper. Biol. & Med. **55**:285, 1944.

4. Curtis, A. H.: Text Book of Gynecology, ed. 5, Philadelphia, W. B. Saunders Company, 1946, p. 555 and p. 557.

5. (*a*) Cattell, R. B., and Swinton, N. W.: New England J. Med. **214**:341, 1936. (*b*) Payne, F. L.: Am. J. Obst. & Gynec. **39**:373, 1940. (*c*) Schmitz, H. E., and Towne, J. E.: ibid. **55**:583, 1948. (*d*) Whorton, L. R.: South M. J. **22**:267, 1929. (*e*) Counseller.[1b] (*f*) Keene and Kimbrough.[1e] (*g*) Turunen.[1g]

1. *Type of Operation.*—In some cases the disease process is so extensive that complete removal of both ovaries or all pelvic organs is necessary and pregnancy could not be expected to occur. In some instances associated pelvic lesions, such as leiomyoma of the uterus, necessitate additional surgical procedures to the extent that the reproductive ability of the patient is destroyed. Only those cases in which the uterus, tubes and enough ovarian tissue for ovulation can be conserved should be considered in the subsequent statistics on "pregnancy possible."

2. *Fertility of the Husband.*—In any survey of sterility the husband is found to be the causative factor in about 30 per cent of cases. In the 18 cases reviewed in this paper the semen of all the husbands was examined prior to the wife's operation. In 3 instances, or 16.6 per cent, the semen was aspermatic. In the existing circumstances pregnancy could not be expected in these 3 cases.

3. *Desire for Pregnancy.*—Three patients with pelvic endometriosis, not included in the present series of 18, were seen and operated on for acquired dysmenorrhea and the reproductive function conserved. When informed that there was a possibility of pregnancy after the operation, all three couples requested contraceptive advice. One of the patients in the present series practiced voluntary contraception for six years before attempting a pregnancy. The practice of voluntary birth control procedures should be taken into consideration in estimating percentages of pregnancy following surgical measures.

4. *Presence of Other Factors Which Might Produce Sterility.*—It has been frequently observed that in many instances of sterility several factors might be present, that each might be a cause of sterility and that the eradication of one factor might not necessarily result in a pregnancy. Cervical erosions, cervical stenosis and hypothyroidism might be, and have been, present in sterile women having endometriosis. Unless these additional factors are treated, an adequate operation for endometriosis may not bring about the hoped-for pregnancy.

Eighteen cases of pelvic endometriosis with a primary or chief complaint of sterility have been studied and are here presented. Dysmenorrhea was present in 3 cases but was not marked. In all 18 complete sterility studies were done on both the husband and the wife.

As mentioned previously, in 3 cases the husbands were found to be sterile. Enough abnormalities were found in the pelvis on pelvic examination in the 3 women to warrant operation, but no promise of subsequent pregnancy was offered.

In the remaining 15 cases operation was undertaken with the hope of a subsequent pregnancy. In addition, all the other possible sterility factors were treated. Eight, or 53.3 per cent, of the patients have become pregnant.

There have been to date 7 full term pregnancies and 1 abortion; 3 women are now pregnant, making a total of 11 pregnancies. One patient became pregnant three times, 1 two times and the other 6 once each.

One patient practiced voluntary contraceptive measures for six years and her husband was overseas in the Army for two and one half years; yet, after his return home she became pregnant in six months when all restrictions were removed. The interval otherwise between operation and the onset of a pregnancy varied from two to ten months, the average being seven months.

TABLE 3.—*Summary of Cases of Patients Becoming Pregnant*

Case No.	Age	Date	Treatment	Time for Pregnancy, Mo.	Outcome
1*	25	11/27/37	Right salpingo-oophorectomy	6	Boy 3/26/47
2	32	4/25/42	Right salpingo-oophorectomy; 75% resection of left ovary	6	Normal boy 10/8/43; normal boy 1/3/46; spontaneous abortion (2 mo.)
3	29	4/24/44	Resection of uterosacral ligaments; suspension of uterus	10	Normal girl 11/3/45
4	24	6/16/46	Resection of uterosacral ligaments; suspension of uterus	5	Boy 8/ 7/47
5	25	10/10/46	Left salpingo-oophorectomy; 50% resection of right ovary; suspension of uterus	5	Girl 12/3/47; pregnant; E.D.C.† 5/5/49
6	26	11/21/46	50% resection of left ovary; suspension of uterus	6	Boy 2/2/48
7	27	9/16/47	50% resection of both ovaries; phenol cauterization of vaginal cul-de-sac implants; suspension of uterus	10	Pregnant; E.D.C. 4/23/49
8	28	5/10/48	50% resection of left ovary; resection of uterosacral ligaments; suspension of uterus	2	Pregnant; E.D.C. 4/23/49

* Practiced voluntary contraception for 6 years because of economic reverses; husband was then in the armed forces for 2½ years.
† Estimated date of confinement.

TREATMENT

The patient with a primary complaint of sterility and for whom a diagnosis of endometriosis is made deserves a very complete and careful sterility study. All factors which might play any part in the problem should be evaluated and corrected. The husband should be thoroughly checked before any surgical therapy is attempted for the patient.

At operation the surgeon will be presented with varied and perhaps difficult problems. He should be as radical as necessary but conservative enough to preserve the reproductive capacity of the patient. Partial resection of the ovary or ovaries should be done even if only a small portion of ovarian tissue remains. If one ovary is so badly involved that resection is impracticable and the other ovary is also involved, partial resection of that ovary is almost mandatory.

This is perhaps a controversial point. Payne [5b] has stated, "Conservation, particularly in young patients with preservation of ovarian and if possible menstrual and procreative functions is justified by the results." Curtis [4] condemns conservation on the basis that such "conservation may be followed by a secondary cystic swelling or inadequate estrogenic function from a fragment of ovary may eventuate in endlessly prolonged menopausal symptoms." When reproduction is the goal, the objections of Curtis can be overruled.

The cortex of the ovary should be preserved, and all sutures should be of very fine surgical gut. The uterosacral ligaments are frequently the seat of endometriosis. Resection of these ligaments is not too difficult and should be done.

TABLE 4.—*Summary of Cases of Patients Not Becoming Pregnant*

Case No.	Age	Date	Treatment	Comment
9	27	6/15/41	50% resection of both ovaries	Unable to find cause of continued sterility
10	29	6/ 7/46	Left salpingo-oophorectomy; 30% resection of right ovary	Hysterogram 3/29/47 showed nonpatent tube
11	31	5/15/47	Right salpingo-oophorectomy; suspension of uterus	Unable to find cause of continued sterility
12	27	3/ 3/48	Resection of both uterosacral ligaments	Basal metabolic rate —27%; taking thyroid, 0.13 Gm. daily
13	27	7/20/48	Resection of both uterosacral ligaments	Using contraceptives; husband has returned to school; patient has to work
14	37	7/24/48	Left salpingo-oophorectomy; 25% resection of right ovary	Uterus had several small fibroids; patient had mild depression after operation; no pregnancy yet attempted
15	30	9/25/48	Right salpingo-oophorectomy; 40% resection of left ovary; suspension of uterus	

Retroversion, frequently due to pelvic adhesions subsequent to endometriosis, is to be corrected by a method which will correct the condition and not interfere with a subsequent pregnancy and not permit recurrence of the retroversion following delivery. Suspension of the uterus should be a part of the operative procedure in those instances in which, in the opinion of the operator, postoperative adhesions might form and produce a retroversion.

No patients with endometriosis and a chief complaint of sterility have been treated by me with either high voltage roentgen therapy or testosterone. Payne [5b] reported that there were no pregnancies in his group of patients treated with high voltage roentgen rays. Schmitz and Towne [5c] reported 2 pregnancies in 12 patients treated with irradiation sufficient to produce temporary menolysis. Androgen therapy was also used by Schmitz and Towne [5c] in 15 cases with the idea of carrying

the patient as long as possible before instituting severe procedures. One patient became pregnant,

In my cases an interval of one month was placed on postoperative sexual abstinence. After this initial month, normal sexual relationship was resumed and a pregnancy attempted.

Experience with normal patients and with patients subjected to operation for cure of sterility due to pelvic abnormalities, such as polycystic ovaries or fibromyoma, reveals that the greatest number of pregnancies occur in the fourth to the seventh month after the initiation of coitus. In the present series, the onset of pregnancy occurred on the average at the sixth month after operation or the fifth month after the resumption of normal coitus. Patients should be warned of the time lag, and their mental outlook will be benefited if they realize that a pregnancy will probably not occur immediately. If it does occur earlier than the average, no harm will be done.

An analysis of the cases of the 7 patients that have not as yet become pregnant is presented in table 4; in cases 16, 17 and 18 the husbands were aspermatic.

SUMMARY

Eighteen cases of endometriosis with sterility as a chief complaint have been reviewed. Conservative operation with preservation of the menstrual and reproductive functions was possible in all cases.

When reproduction is the goal of the operation, resection of the ovaries, if they are involved, is justified, even if only a small portion of the ovary remains.

Additional resection of other areas of ectopic endometrium should be done and suspension of the uterus performed.

Further sterility studies revealed the husband to be the causative factor in 3, or 16.6 per cent, of the cases.

Of the remaining 15 cases, in 8, or 53.3 per cent, the patient has become pregnant; there has been a total of 11 pregnancies to date.

DISCUSSION ON PRECEDING PAPERS

DR. EGBERT H. FELL, Chicago: I wish to comment briefly regarding the very excellent presentation by Drs. Julian and Metcalf. In the past few months my colleagues and I have been using the same type of clamp in the experimental laboratories (on dogs) and in the necropsy laboratories and believe, as the authors do, that it is going to be a great help in the type of procedure that they have discussed. I am sure that it will cut down on the time interval which Dr. Blakemore and others have reported. I should like to ask that Dr. Julian state how long his procedure took. I believe, from our work in the laboratory, that the approach through the chest and abdomen would also be of help in this procedure. It, too, will give better access to the vessels, and with the aid of this new clamp the operation will be of shorter duration and much more easily accomplished.

DR. THOMAS C. DOUGLASS, Chicago: I agree entirely with what Dr. Julian and Dr. Fell said about the use of this clamp. My colleagues and I have been running an experiment recently on the cause of closure of these shunts in the laboratory, using the same clamp. It certainly is a very handy device and makes the operation very simple. I am not so sure that the disadvantage of the clamp mentioned by Dr. Julian—that is, the impossibility of using an everting type of suture in doing the anastomosis—is a disadvantage. Certainly, in the dogs we have had the healing of the shunt has been quite satisfactory. As a matter of fact, without obstructions of the portal vein proximal to the anastomosis, most of these shunts will close. If the portal vein is obstructed, however, they remain open for a prolonged period. I believe also that the approach through the abdomen, as Dr. Julian has shown, is quite a satisfactory approach, but we have not yet had the opportunity to do the operation on a human patient. I believe it can be done very simply and in much shorter time than has been reported by Blakemore and others.

DR. WALTER G. MADDOCK, Chicago: I should like to ask Dr. Ormond to say more about the treatment of the shock kidney. It is perfectly true that my experience in the past has been that in dealing with severe burns the administration of large amounts of fluid has often not resulted in a good urine output. On the other hand, it is a bit dangerous when considering any patient with oliguria or anuria not to consider a plentiful supply of water as the best diuretic. I am sure fluids are often pushed too far; hence I should like Dr. Ormond to tell just what measures should be taken to see that the patient has sufficient water and yet not too much.

DR. JOHN K. ORMOND, Detroit: First, I think it must be remembered that this concept of the lower nephron nephrosis is still not completely proved. It is still somewhat provisional, although we get more and more evidence in our pathologic studies and our autopsies that it is basically correct. If it is correct, the pouring in of fluids can do no good whatsoever. The necrosis of the cells of the ascending limb of the loop of Henle prevents the selective action of those tubes, and the fluid which is secreted or filtered by the glomeruli is passed down the tubes, just as it was before; but, since the power of selective resorption has been abolished, all that fluid is either poured back directly into the veins or resorbed into the veins, with the result that there is no possibility of the urine getting through. If that theory is correct—and it seems to have a great deal of backing—then in no circumstances in which this condition is present can the pouring in of the fluids do more than overload the circulation.

Another question was brought up, about burns. When I wrote my paper on this subject, I included thermal burns as one of the causes of this lower nephron nephrosis. Dr. Lam, who is a member of this organization at our hospital, said, "Burns do not cause this. What causes it is the tannic acid that has been used."

DR. WALTER G. MADDOCK, Chicago: Dr. Ormond, what are your indications for starting the use of the gastric lavage? When do you start it in the treatment, and just what methods do you use?

DR. JOHN K. ORMOND, Detroit: In a good many of our patients we have had to start gastric lavage on account of the presence of distention, etc., and the nasal tube is passed. We have taken advantage of that to use the gastric lavage. The chief indication, however, is the increasing toxemia. I do not believe that anybody knows when toxemia becomes dangerous. Nobody knows whether it is the nitrogen or the accompanying production of cellular metabolism that is poisonous. I only

know that the nitrogen acts as an indication, like the level of mercury in a thermometer. As I say, our experience is small. We pass the tube when the nonprotein nitrogen level is 100 mg. or a little higher. We do not pay much attention whether it gets down into the duodenum or whether it stays in the stomach. We inject fluids and then withdraw by suction, measuring the amount put in and the amount withdrawn, and then we subtract the amount withdrawn from the amount that was put in, and use that in our calculations of the amount of fluid that the patient is obtaining. In 1 patient we measured the nonprotein nitrogen content of the gastric lavage and found on one occasion that it was 66.5 mg. per hundred cubic centimeters. In another we found that it was 46.5 mg. These are the levels in the fluid extracted from the stomach by suction.

DR. O. C. JULIAN, Chicago: I want to thank Dr. Fell and Dr. Douglass for their comments. The approach through the abdomen is adequate in a thin person. Our patient was thin. If the patient is obese, and many of them are, I believe that the thoracoabdominal approach will be needed. The disadvantage of the thoracoabdominal approach in a patient with hepatic disease is that the liver will be enlarged occasionally, and there will be difficulty in displacing it up into the chest to expose its under surface. The time of operation was four and one-half hours in the case reported. I might say that we were misled in thinking that we had discovered a new syndrome. In palpating the liver and the tissues about the false ligament, a continuous bruit was palpated that was most striking, beyond any vascular bruit in a normal area that I had ever experienced, and much time was spent in trying to find an arteriovenous aneurysm.

I agree with Dr. Douglass that possibly the disadvantage of an over-and-over suture is overemphasized. However, one has only one opportunity in any patient to do this procedure, and I believe that the very best possible procedure would be to use an everting suture when it is made possible by a deeper clamp.

DR. J. GRAFTON LOVE, Rochester, Minn.: Patients such as Dr. Erb and I reported on are not encountered frequently and an operation will not be required very often, but when it is required it seems to me we have a procedure which will mean much to a few patients. I believe that it would be wise to administer streptomycin to these tuberculous patients before operation and to keep administering it to them for a long period afterward. How big a part streptomycin plays in the healing of the bone in these cases I do not know, but I think that we should give it credit for a good part of the successful outcome after the operation.

SURGICAL TREATMENT OF TRICUSPID ATRESIA

EGBERT H. FELL, M.D.
BENJAMIN M. GASUL, M.D.
CARL B. DAVIS Jr., M.D.
AND
RAUL CASAS, M.D.
CHICAGO

WILLIS POTTS and Sidney Smith [1] added an important chapter in the treatment of tetralogy of Fallot to that which Blalock and Taussig [2] so well began. The Potts-Smith operation, a lateral anastomosis of the pulmonary artery to the aorta, establishes an artificial ductus arteriosus, thus utilizing vessels that are accessible and large enough so that the infant under the age of 2 years who heretofore died of severe oxygen want now has a chance to live. It has been stated that there is a greater mortality in the group awaiting operation than in the operative and postoperative group.

The favorable results we have had with the Potts-Smith procedure in the age group from 4 to 12 months encouraged us to attempt this operation on 3 very small, cyanotic infants with diagnoses of congenital tricuspid atresia, or nonfunctioning right ventricle. There have been other cases of tricuspid atresia reported but we believe none in which operation was done at such an early age as in those to be reported here.

Congenital tricuspid atresia is rare.[3] There were 5 infants with this condition in the group of 135 with congenital cardiac anomalies studied in the children's cardiac service of the Cook County Hospital this past year. Thirty-three of the 135 anomalies were amenable to

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Read at the Sixth Annual Meeting of the Central Surgical Association, Feb. 18, 1949.

From the Cardio-Vascular Service of the Cook County Children's Hospital and the Laboratories of the Presbyterian Hospital.

1. Potts, W. J.; Smith, S., and Gibson, S.: Anastomosis of Aorta to Pulmonary Artery, J. A. M. A. **132**:627 (Nov. 16) 1946.

2. Blalock, A., and Taussig, H.: Surgical Treatment of Malformations of Heart in Which There Is Pulmonary Stenosis or Pulmonary Atresia, J. A. M. A. **128**:189 (May 19) 1945. Blalock, A.: Surgical Procedures Employed and Anatomical Variations Encountered in Treatment of Congenital Pulmonic Stenosis, Surg., Gynec. & Obst. **87**:385 (Oct.) 1948. Taussig, H. B.: Congenital Malformations of the Heart, New York, Commonwealth Fund, 1947.

3. Alexander, F., and White, P.: Four Important Congenital Cardiac Conditions Causing Cyanosis to be Differentiated from Tetralogy of Fallot; Tricuspid Atresia, Eisenmenger's Complex, Transposition of Great Vessels and Single Ventricle, Ann. Int. Med. **27**:64 (July) 1947. Abbott, M.: Atlas of Congenital Cardiac Disease, New York American Heart Association, 1936. Blackford, L. M.,

(Footnote continued on next page)

surgical correction; 3 of these were tricuspid atresia. The life expectancy is usually less than one year and depends on the patency of the ductus, anomalous arterial supply to the lungs and interauricular and interventricular septal defects. The success of the operation, likewise, depends on the continuance of the interauricular septal defect. An associated interventricular septal defect and patent pulmonary artery may also prolong life.

The blood flow in an infant with tricuspid atresia is from the right auricle through the interauricular septal defect to the left auricle, to the left ventricle and thence to the aorta (fig. 1). As long as the ductus arteriosus remains patent, blood will reach the lungs and the infant may appear normal, but as the ductus closes cyanosis increases in severity.

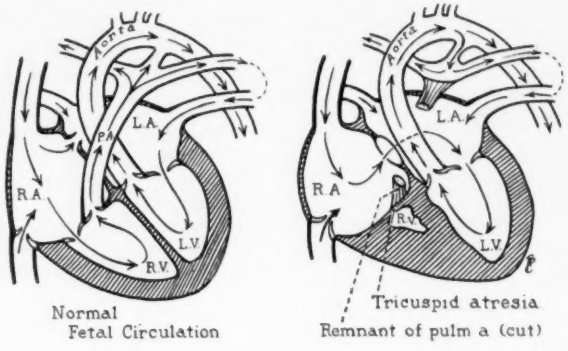

Fig. 1.—*A*, the normal fetal or newborn circulation; *B*, the circulation in the heart and great vessels in the presence of tricuspid atresia, interauricular septal defect and patent ductus arteriosus.

The diagnosis of nonfunctioning right ventricle is made by the appearance of cyanosis, which is usually seen earlier in infancy and is severer than that seen in an infant with the tetralogy of Fallot. Fluoroscopic examination reveals a boat-shaped heart of normal size with a small right ventricular shadow while the left ventricular shadow is increased; there is a pulmonary window and lack of pulmonary conus.

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and Hoppe, L. D.: Functionally Two-Chambered Heart, Am. J. Dis. Child. **41**:1111 (May) 1931. Bellet, S., and Stewart, H. L.: Congenital Heart Disease: Atresia of Tricuspid Orifice, ibid. **45**:1247 (June) 1933. Gibson, S., and Clifton, W. M.: Congenital Heart Disease, ibid. **55**:761 (April) 1938. Taussig, H. B.: Analysis of Malformations of Heart Amenable to Blalock-Taussig Operation, Am. Heart J. **36**:321 (Sept.) 1948. Taussig, H. B.: Clinical and Pathological Findings in Congenital Malformations of Heart, Bull. Johns Hopkins Hosp. **59**:435 (Dec.) 1936.

The electrocardiogram shows a left axis deviation in contrast to the right axis deviation that is characteristic of the tetralogy of Fallot. The blood picture is similar to that in the tetralogy in that in both there is a marked increase in red blood cells and hemoglobin content and a low arterial oxygen content which is further diminished by the exercise test.

In the 3 cases to be reported there were all the diagnostic criteria (previously mentioned), and, in addition, the conditions were so severe that continuous administration of oxygen was essential for life from the time that the patient was first seen until operation was done. Parenteral

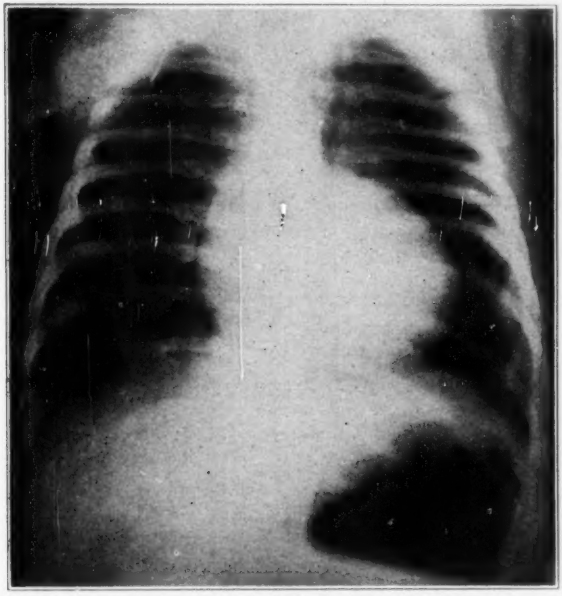

Fig. 2 (case 1).—Anterior-posterior view of the chest, showing clear pulmonary fields, boat-shaped heart, enlarged left ventricle and absence of the shadow normally caused by the pulmonary artery.

administration of food or fluids was necessary to overcome the frequent periods of unconsciousness that took place when food was given orally. All personnel who helped care for the infants believed that they would die at any moment.

We did not believe that operation would be possible; yet it held the only hope of providing the lungs with blood and affording an opportunity for life. The anesthesia was administered by Dr. F. M. Grem, chairman of the department of anesthesia of the Cook County Hospital, and the Potts-Smith procedure was completed without difficulty in each case. The anastomotic openings did not exceed 4 mm.

Postoperatively the patients were placed in oxygen tents for four or five days, and in due time were discharged to their homes with good color, gaining in weight and returning to normal activity for infants of their age.

REPORT OF CASES

CASE 1.—A 3 month old white boy was admitted to the cardiac service of the Cook County Children's Hospital on April 23, 1948, with the presenting complaint of cyanosis which was noted three days after a normal birth. His weight at birth was 5 pounds 3 ounces (2,355 Gm.). Seven and one-half weeks after birth, because of severe episodes of cyanosis, unconsciousness and marked dyspnea, he was hospitalized and oxygen was administered. He was transferred to the pediatric service of the University of Illinois on April 1, 1948.

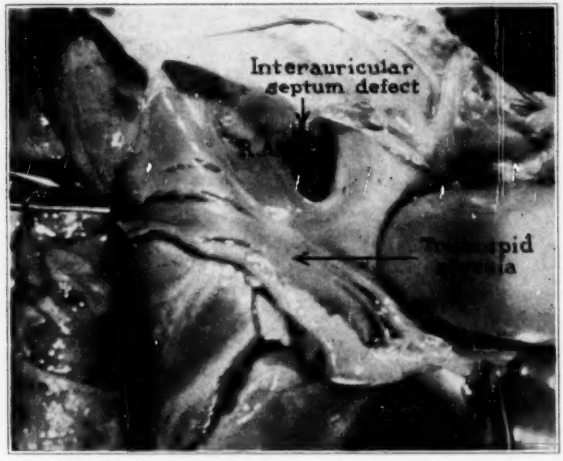

Fig. 3 (case 1).—A large interauricular septal defect leading from the right auricle is evident. There is no tricuspid valve or communication with the right ventricle. There was no evidence of failure of the right side of the heart.

Examination by one of us (B. M. G.) at this time revealed a 3 month old infant in distress, crying and gasping for air, with intense cyanosis of hands, feet, lips and mucous membranes. Respirations were 60 per minute with suprasternal retractions. The pulse rate was 160 and regular; the blood pressure was 76 systolic and 40 diastolic. The femoral pulse was present. Administration of oxygen did not completely relieve the cyanosis. The apex beat was in the fifth interspace, just outside the midclavicular line. There was a harsh systolic murmur, best heard in the second interspace on the left. There was no pulsation of the liver.

Fluoroscopic examination revealed the base of the heart to be markedly narrowed; there was a concavity in the region of the pulmonary conus with absence of pulmonary pulsations, and the pulmonary fields were clear. In the left oblique view, the left ventricle was definitely enlarged and the right ventricle

was small and was unusually distant from the anterior wall of the chest. The pulmonary window was wide and clear. There was a left aortic arch.

The electrocardiogram revealed a left axis deviation. Examination of the blood showed a hemoglobin content of 15 Gm., 7,970,000 erythrocytes and 10,650 leukocytes.

A diagnosis of tricuspid atresia was made, and the infant was transferred to the cardiac service of the Cook County Children's Hospital for further study and possible operation.

Fig. 4.—Upper illustration, a very small right ventricle is exposed, from which leads a small nonfunctioning pulmonary artery. There is no communication between the right ventricle and either the right auricle or the left ventricle. The left ventricle is noticeably hypertrophied. Lower illustration, the interior of the left side of the heart is shown. The interauricular septal defect is large and patent; the left ventricle is large and the wall hypertrophied.

Dextroangiocardiograms were interpreted as showing incomplete filling of the right ventricle, absence of a pulmonary artery and filling of the left auricle and of a large part of the left ventricle.

The diagnosis of tricuspid artresia with an interauricular septal defect, pulmonary stenosis and either a patent ductus or an interventricular septal defect was made.

From April 23 to July 2, the infant did very poorly, in spite of continuous administration of oxygen. Stimulants were used at times to aid in restoring consciousness.

Preoperatively, as in all cases of cyanosis, the patient was well hydrated. Atropine sulfate, 1/500 grain (0.4 mg.) preceded the cyclopropane-oxygen anesthesia. The chest was entered laterally through the fourth interspace. A quill-sized pulmonary artery was anastomosed to the aorta according to the method described by Potts and Smith. The anastomosis was 4 mm. in length. The

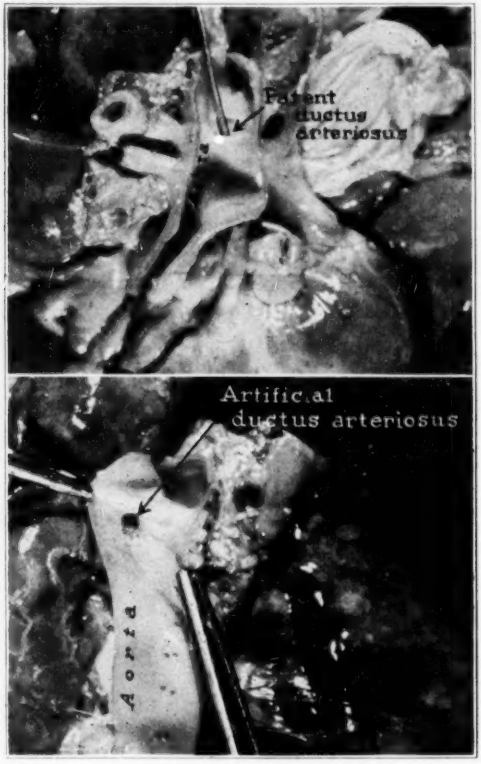

Fig. 5.—Upper illustration, the aortic arch has been opened, and a fine probe introduced into a small patent ductus arteriosus. Very little benefit was derived from this ductus. Lower illustration, the aorta distal to the left subclavian artery is opened and shows the artificial ductus between the aorta and pulmonary artery. The anastomosis was patent and appeared to have been functioning satisfactorily.

wound was closed in layers and the chest drained through a water seal for twenty-four hours.

The patient received 100 cc. of saline solution and 150 cc. of plasma during the operation; parenteral administration of food and fluids was continued for the first thirty hours, and thereafter he was fed by mouth. Oxygen was not

administered after the fifth postoperative day. On the sixteenth postoperative day he was found to have chickenpox and was transferred to the Contagious Division of the Cook County Hospital, where he made a successful recovery. He was discharged to his home on August 3, eating well, having good color and weighing 9 pounds 15 ounces (4,500 Gm.), 1¼ pound (570 Gm.) more than he weighed when he was operated on. The stethogram showed the presence of a continuous murmur which could be easily heard, and the blood count was within normal limits.

The patient was seen at intervals in the outpatient clinic, and his color was noted to be normal and there was a satisfactory gain in weight and activity. On Jan. 15, 1949, a little over six months after operation, he was admitted to the Cook County Children's Hospital with severe bilateral bronchopneumonia and died within twelve hours of admission. Postmortem examination showed tricuspid atresia, a large interauricular septal defect, a ductus arteriosus with a very small lumen and a satisfactory-appearing artificial ductus between the aorta and the left pulmonary artery. There were pulmonary stenosis and hypertrophy of the left ventricle. There was no evidence of cardiac decompensation, endocarditis or aortitis, nor was there an interventricular septal defect.

From our postmortem studies, we believe that this patient with a completely nonfunctioning right ventricle and a large interauricular septal defect had an efficiently functioning heart and the cause of death was not related to the congenital cardiac condition or the surgical procedures associated with it.

Case 2.—A 5½ week old white boy was admitted to the cardiac service of the Cook County Children's Hospital on July 21 1948, with the presenting complaints of dyspnea, rapid respirations of five weeks' duration and attacks of intermittent cyanosis of three weeks' duration.

His weight was 6 pounds 7½ ounces (2,900 Gm.) following a normal delivery. Labored rapid respiration was noted at this time. The physical examination revealed a 5½ week old cyanotic infant, weighing 6 pounds 11 ounces (3,034 Gm.), with severe dyspnea. Respirations were 70 per minute, pulse rate 160 and blood pressure 65 systolic and 25 diastolic. There was a marked cyanosis of all mucous membranes, fingers and toes and, to a slightly less degree, over the rest of the body. The femoral pulse was palpable.

The apex of the heart was in the fourth left interspace, just outside the midclavicular line. There was a harsh systolic murmur heard over the precordium. The liver was palpable, and at times a pulsation of its edge was questioned. The hemoglobin level was 18.5 Gm., the erythrocyte count was 6,500,000 and the leukocyte count was 12,000.

The fluoroscopic examination revealed in the posterior-anterior view a narrowing of the base of the heart. The pulmonary conus showed a straight, flat line. The pulmonary fields were unusually clear, with no pulsations of the pulmonary vessels. The left oblique view showed an enlarged left ventricular shadow and a diminished shadow in the right ventricular area. The pulmonary window was clear; the esophagram demonstrated a deviation associated with a normally placed aortic arch and descending aorta.

The electrocardiogram showed a sinus tachycardia and a left axis deviation.

A diagnosis of tricuspid atresia, or nonfunctioning right ventricle, with associated essentials—an interauricular septal defect and poorly functioning ductus arteriosus or an interventricular septal defect—was made.

In spite of continuous administration of oxygen, the infant had severe attacks of cyanosis and periods of unconsciousness. His cyanosis increased with age to a point that he could not take foods or fluids by mouth. With the use of blood and fluids intravenously, his weight was brought up to 7 pounds 1 ounce (3,200 Gm.) on August 6, the day of operation. Atropine sulfate 1/480 grain (1.2 mg.) was given preoperatively to aid in the administration of cyclopropane-oxygen intratracheal anesthesia. A Potts-Smith operation was completed through the fourth interspace of the left side of the chest; the anastomosis was 3 to 4 mm. in length. A good loud machine-like murmur was present directly

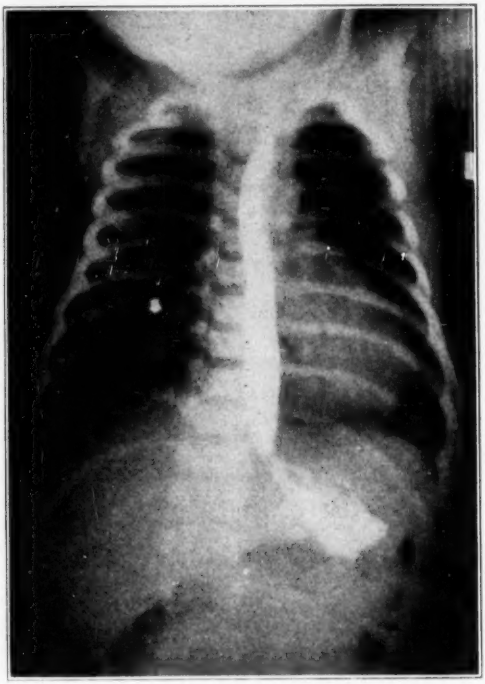

Fig. 6 (case 2).—Roentgenograms of the chest and esophagram of a 7½ week old infant. The esophagram gives evidence of a left aortic arch. The pulmonary fields are clear and free of pulmonary vessel markings. The heart is boatlike in shadow, and there is a lack of a pulmonary artery shadow.

after operation and the infant was put into an oxygen tent for four days; food was taken by mouth thirty-six hours postoperatively. He was discharged twenty-three days after operation, having gained in weight and with a normal blood picture. A continuous murmur was best heard to the left of the sternum in the fourth interspace.

Case 3.—A 10 week old white boy was admitted to the cardiac service of the Cook County Children's Hospital on Feb. 13, 1949, very cyanotic. The child had been delivered by cesarean section and weighed 7 pounds 6½ ounces (3,360 Gm.).

Cyanosis was first noted at 3 weeks of age, at which time his physician stated that the infant had heart trouble. The cyanosis increased gradually, and on admission he had marked cyanosis associated with rapid respirations and cough, the last two complaints having been particularly noticeable in the past two weeks.

The physical examination showed a well developed baby weighing 9 pounds 8 ounces (4,310 Gm.). The marked cyanosis was increased in severity on crying or straining.

The lungs were clear. No cardiac murmurs were heard. The liver was not enlarged, nor was any pulsation of it noted. There was a good femoral pulse bilaterally. The respiration rate was 50 per minute, pulse rate 135 and temperature 98.3 F. The hemoglobin content was 16.5 Gm., erythrocytes 6,100,000, and leukocytes 12,250.

The roentgen and fluoroscopic examinations revealed a small right ventricle, a large left ventricle, a wide pulmonary window, decreased vascular markings and a concavity in the region of the pulmonary artery. The esophagram was compatible with a left aortic arch. The electrocardiogram revealed a left axis deviation and a sinus tachycardia.

The child was in a semicomatose state in spite of the fact that oxygen was continuously administered. Because of the favorable results in the 2 previous cases and the fatal termination if left alone, operation was advised. On Feb. 16, 1949, a 4 mm. anastomosis was made between the aorta and the left pulmonary artery. The infant made a spectacular recovery and was discharged thirteen days after the operation, weighing 1 pound (450 Gm.) more than at the time of operation and having a normal blood picture. The postoperative management and course were similar to those in the previous cases.

SUMMARY AND CONCLUSIONS

Three infants, aged 7½ weeks (weighing 7 pounds, 1 ounce), 5½ months (weighing 8 pounds) and 10 weeks (weighing 9 pounds, 1 ounce) with severe increasing cyanosis due to congenital tricuspid atresia were successfully operated on by the Potts-Smith procedure.

We do not advocate early operation for tetralogy of Fallot or tricuspid atresia unless it is evident that the patient will not survive conservative therapy. The 3 cases reported lead us to believe that we have waited too long and have been influenced too greatly by authors who have stated that operation should not be done before the age of 2 years. The Potts-Smith operation is a procedure that may be used on the very small infant. Time alone will tell whether this procedure will be of permanent benefit.

Severe cyanosis occurring in infancy associated with an enlargement of the left ventricle, diminution of the right ventricle and a left axis deviation as evidenced by the electrocardiogram are indicative of a tricuspid atresia. The life expectancy is less than one year. The group of patients with this defect is small but if the diagnostic criteria are kept in mind, relief is possible through surgical measures if there are no other congenital abnormalities to contraindicate an operative procedure.

TRACHEOESOPHAGEAL FISTULA CAUSED BY BLUNT VIOLENCE

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AND
R. K. GILCHRIST, M.D.
CHICAGO

THE PRESENT report deals with a case of tracheoesophageal fistula resulting from a severe blow over the sternum. This condition is extremely rare, and in a search of the literature only 2 similar cases with recovery were found. One of these, like the present case, presented no evidence of accompanying fracture of the ribs, cartilages or sternum. Both of the other cases were apparently reported twice.

The relative frequency of tracheoesophageal fistula based on etiology is furnished by Mangabeira-Albernaz,[1] who in 1933 studied 682 cases collected from the world literature. His classification of these fistulas is given in the table.

REPORT OF A CASE

History.—On March 30, 1947, a 29 year old man was brought to the hospital by the police about fifteen minutes after injury. The patient stated that while driving home after having had some drinks he fell asleep at the wheel and his car struck the rear of a parked car. In the crash the steering wheel was broken by the impact of his chest. He had been in good health prior to his injury.

Physical examination revealed a well nourished white man of 29 years, alert, cooperative and not in shock. The blood pressure was 120 systolic and 80 diastolic. Temperature, pulse and respiration were normal. No significant abnormalities were noted except for pain on pressure over the left upper part of the thorax and persistent expectoration of bloody mucus. There was no bruise or abrasion anywhere on the thorax. Examination of the oral cavity and the nasopharynx did not reveal the source of bleeding.

Diagnosis.—It was thought at first that the patient had sustained fractured ribs and associated injury to the lung, and therefore treatment with penicillin, 20,000 units every three hours intramuscularly, was started. Roentgen examination of the chest revealed no abnormalities. It was later observed that whenever the patient attempted to take food or drink he was seized with paroxysms of coughing and vomiting. Roentgen examination of the chest during ingestion of iodized oil

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From the service of Dr. R. K. Gilchrist, Surgical Department, Cook County Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Mangabeira-Albernaz, P.: Ann. d'oto-laryng. **8**:889 (Aug.) 1933.

U. S. P. (lipiodol®) demonstrated a communication between the esophagus and trachea in the region of the tracheal bifurcation.

Management.—It seemed that successful closure of the fistula in the present case depended, first, on control of infection at the site of injury and, second, on maintenance of nutrition and hydration. Use of penicillin was continued for three months. Fluid balance was maintained by parenteral administration of fluids at the beginning. Sodium sulfathiazole was given in the intravenous fluids intermittently. On the fifth day a Levin tube was passed into the stomach, and thereafter high protein, high vitamin feedings were given by tube.

Progress.—The patient did reasonably well on the management outlined, but some difficulties were encountered. On one occasion he vomited after a tube feeding, and shortly thereafter chill and fever (temperature up to 101 F.) developed. Fortunately, after removal of the Levin tube and treatment with intravenous injectons of sodium sulfathiazole, the symptoms subsided. Also the

Etiologic Classification of Tracheoesophageal Fistulas (According to Mangabeira-Albernaz [1])

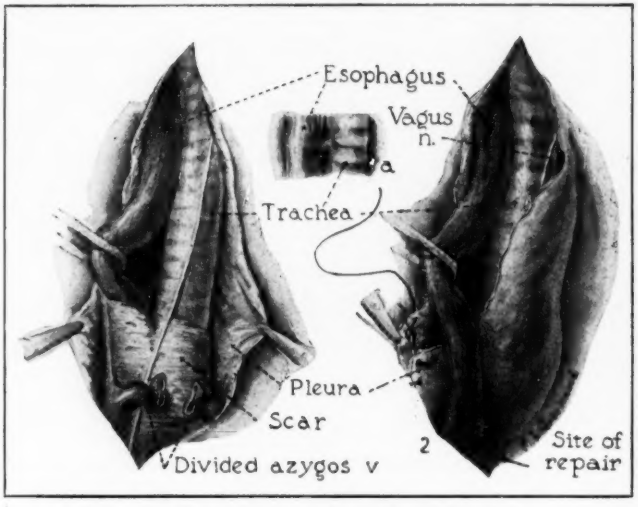
Cause		Number of Cases
Congenital		222
Mixed congenital		3
Neoplastic		367
Infectious (nonspecific)		1
Infectious (specific)		40
Syphilis	24	
Tuberculosis	14	
Actinomycosis	2	
Traumatic		40
External foreign bodies (gunshot wounds)	5	
Internal foreign bodies (fishbones)	22	
Decubitis ulcer (in a case of substernal goiter)	4	
Operative	1	
Following rupture of aneurysm	5	
Following esophageal stenosis	3	
Undetermined cause		2
Cause not specified		7
Total		682

patient was becoming less tolerant of the nasal tube, and, despite calculated adequate food intake, he lost 24 pounds (10.9 Kg.) in twenty-one days. Therefore a gastrostomy was done on April 21, 1947. Thereafter his strength and state of mind improved considerably. However bronchoesophagoscopy on June 28, approximately three months after injury, revealed a 3 mm. slit about 24 to 27 cm. from the incisor teeth "with edges smooth and epithelized."

Preoperative Status.—Immediately before surgical repair of the fistula was undertaken, the patient was in good condition. His weight was 160 pounds (72.6 Kg.); the erythrocyte count was 4,120,000; the hemoglobin level was 13.5 Gm. (normal 15.6 Gm.—100 per cent), and the leukocyte count was 12,800. The total serum protein level was 7.0 Gm. per hundred cubic centimeters of whole blood. Repeated roentgen ray studies revealed the persisting communication between the esophagus and trachea in the vicinity of the bifurcation. Administration of penicillin, 20,000 units every three hours, was begun the day before operation.

Surgical Repair.—Three months and eleven days after injury, with use of intratracheal cyclopropane-ether anesthesia, the right side of the chest was opened by removing the fourth rib from its bed. The azygos vein was doubly ligated

and divided between ligatures. The esophagus and trachea above the level of the lesion were exposed by incision of the pleura, and the interval between the two structures was carefully developed downward to the site of pathologic change, marked by dense scar tissue. The fistulous tract was exposed and divided. It was more than 1 cm. in its long diameter and was completely epithelized. The defects in the trachea and esophagus were closed in two layers with fine continuous chromic surgical gut sutures. A flap of mediastinal pleura was turned and placed so that it separated the suture lines in the trachea and esophagus. The mediastinal pleura was not closed. Closed drainage of the thorax was provided by means of an intercostal catheter in the dependent portion of the lateral chest wall. The chest was closed with interrupted chromic surgical gut sutures. During and immediately after operation the patient received 1,500 cc. of whole blood through cannulas in both ankle veins.



Surgical repair of tracheoesophageal fistula.

Postoperative Course.—The patient was given oxygen by nasal tube. Continuous suction through the gastrostomy opening was established. Besides penicillin, sodium sulfathiazole was given in parenterally injected fluids. On the third postoperative day the intercostal catheter was not functioning. Roentgen examination showed collapse of the middle and lower lobes of the right lung and evidence of air under tension. The catheter was removed and a thoracentesis was done for removal of air. On the fourth postoperative day another catheter was reinserted into the thorax through a new site. On the seventh postoperative day culture of the drainage showed colon bacilli and some hemolytic streptococci.

In the following days the patient had a septic fever and was very toxic, and the catheter drainage was inadequate. On the twenty-second postoperative day a thoracostomy was done by removal of a section of the tenth rib in the posterior axillary line. Evidently the patient had been eating despite advice to the con-

trary, for at operation the pulp of an orange was removed from the pleural cavity. The skin margins of the wound were sutured to the thick pleura to prevent premature closure of the opening. With open drainage established, the patient's condition improved and the empyema cavity decreased in size. He became dissatisfied, however, and absconded from the hospital before further evaluation of his status could be made.

Six months later the patient was persuaded to return to the hospital, and he was admitted on March 24, 1948. Physical examination revealed a functioning gastrostomy opening. Temperature, pulse, respiration and blood pressure were within the range of normal. A roentgenogram of the chest showed obliteration of the right costophrenic sinus. A calcified plaque was present in the same area. Results of routine laboratory studies were normal. Two days after admission the gastrostomy opening was closed under cyclopropane-ether anesthesia. The patient had a mild infection of the wound but was well enough to leave the hospital on his fifteenth postoperative day.

COMMENT

The present case presents several interesting features, the first of which is that tracheoesophageal fistula may occur from blunt violence, without demonstrable injury to the thoracic cage and without emphysema. In this case and in 2 other similar cases, previously mentioned and abstracted at the end of this article, the fistulas occurred in the region of intimate contact between the trachea and the esophagus, in the vicinity of the tracheal bifurcation.

Mediastinitis and early death were probably averted by early use of penicillin along with chemotherapy. Withholding of all oral intake and substituting feeding by the Levin tube and, later feedings through the gastrostomy opening were necessary adjuncts in the prevention of mediastinal infection as well as in building up the patient for reparative surgical procedures. It seems to us that feeding through an early gastrostomy opening is preferable to continued feeding by Levin tube.

While conclusions regarding the most satisfactory method of handling this type of case are not justified, it seems that surgical division of the tract is indicated as soon as the inflammation at the site of injury has subsided. The interposition of a flap of mediastinal pleura between the sites of repair of the two structures is recommended to lessen the chances of recurrence.

In connection with definitive treatment of tracheoesophageal fistula generally, it should be added that cases of successful closure of certain types of fistulas by endoscopic treatment of the area with caustics have been reported.[2] Spontaneous closure has also been reported.[3]

After surgical closure of the fistula has been accomplished, it is necessary to withhold food and drink by mouth until complete healing

2. Abbott, O. A.: J. Thoracic Surg. **14**:382 (Oct.) 1945. Clerf, L. H.: Ann. Otol. Rhin. & Laryng. **42**:920 (Sept.) 1933.

3. Rucks, W. L.: Memphis M. J. **7**:209 (Nov.) 1930.

has occurred. The surreptitious taking of food by the patient in the present case led to breakdown of the esophageal repair with consequent development of empyema, resulting from the collection of food material in the pleural cavity. It is remarkable how drainage of the empyema and the following expansion of the lung were effective in bringing about closure of the esophagopleural communication.

SUMMARY AND CONCLUSIONS

On the basis of this study, the following points appear to us to be of utmost importance as requisites for successful management.

1. Tracheoesophageal fistula occurring near the bifurcation of the trachea may result from steering wheel injuries. There may be no injury to the chest wall, nor need there be emphysema or severe shock.

2. The diagnosis should be considered whenever the patient has fits of coughing on taking food or drink. Confirmation is obtained by esophagoscopy and bronchoscopy together with roentgen study of the chest following ingestion of radiopaque material.

3. Chemotherapy and antibiotics aid in preventing infection.

4. Oral feeding is contraindicated.

5. Gastrostomy should be done as soon as practicable. In this case it was not done until three weeks of feeding by Levin tube had proved unsatisfactory.

6. The fistula is repaired through a right thoracotomy. Interposition of a flap of mediastinal pleura between the sites of repair is probably useful in preventing recurrence.

7. Underwater drainage of the thorax is recommended.

8. Postoperatively oral intake should be withheld until healing has been assured.

ABSTRACTS OF SIMILAR CASES FROM THE LITERATURE

1. Piquet, Muller, Marchand and Decoulx [4] report the case of a 31 year old man who was crushed against a wall by a machine and sustained fractures of the left third to fifth ribs at the "level of their anterior arcs" and fracture of the mandible. On the third day after injury, coughing occurred on attempts to take food or drink. The patient eventually learned to bend to the left when eating or drinking and in this manner abolished the associated spasms of coughing. Fluoroscopically, about one month later, ingested barium sulfate solution was seen to fill the right lower bronchus, establishing the presence of a broncho-esophageal fistula in the region of the bifurcation of the trachea. Broncho-esophagoscopy five months after injury revealed much scarring in the esophagus and in the right main bronchus. Roentgen examination several days later again revealed the fistula, which was not actually seen by endoscopy. The authors

4. Piquet; Muller; Marchand, and Decoulx: Ann. méd. lég. **19**:125 (Feb.) 1939.

expressed the opinion that the fistula resulted from trauma, which probably brought about the rupture into the trachea of a preexisting traction diverticulum of the esophagus. The possibility of an asymptomatic congenital fistula as a basis for development of the fistula after trauma is dismissed by the authors as very unlikely, since very few instances of asymptomatic congenital fistulas have been observed. The treatment and eventual outcome are not reported.

2. Adams and Mabley [5] report the case of a 19 year old youth who was struck on the chest by a 700 pound (318 Kg.) box which had fallen 10 feet (3 M.). The patient had emphysema of the neck and face but not of the chest wall. He was in shock and presented evidence of laryngeal obstruction which necessitated tracheotomy. A Levin tube was passed into the stomach but did not prove satisfactory, and a gastrostomy was done. Thereafter the patient improved rapidly. Bronchoesophagoscopy revealed a large tracheoesophageal fistula just above the level of the carina. Approximately four months after the injury, the fistula was excised and the defects in the trachea and esophagus were closed. The chest was closed without drainage. Penicillin was given before and after operation. The postoperative course was uneventful, and on the fourteenth postoperative day the patient was able to eat a normal diet and to be up. In this case, despite the severe trauma, fracture of ribs, sternum or cartilages could not be demonstrated.

5. Adams, H. D., and Mabley R. E.: J. Thoracic Surg. **15**:290 (Aug.) 1946.

AN EXTRAVESICAL METHOD FOR THE RELIEF OF VESICAL OCCLUSION

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AND
STEPHEN BURDON, M.D.
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MR. TERENCE MILLIN'S method of extravesical prostatectomy has proved its merit clinically in the past three years. The retropubic approach is fundamentally not a new procedure, but Mr. Millin has developed it as a simple and successful method. We will discuss briefly the technic,[1] will recount our experience with retropubic prostatectomy [2] and will report the application of the retropubic approach in the treatment of obstructions of the vesical neck in infants and children.

The retropubic prostatectomy employs extravesical approach to the prostate gland, which is, though seemingly infrequently appreciated, an extravesical structure. In other words, by this approach one does not go through the bladder to attack a pathologic condition that lies outside the bladder, as is commonly practiced in the popular Freyer, or suprapubic, method.

The prostate is exposed through either a longitudinal or a transverse suprapubic incision which includes both skin and fascia of the rectus muscles. The rectus muscles are separated, the hypogastric facia opened

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Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Millin, T.: Retropubic Prostatectomy, Lancet **2**:693-696, 1945; Retropubic Prostatectomy, J. Urol. **59**:267-280, 1948; Retropubic Urinary Surgery, Baltimore, Williams & Wilkins Company, 1947. Grant, O.; Lich, R., Jr., and Maurer, J.: Retropubic Prostatectomy, Urol. & Cutan. Rev. **52**:9-12, 1948. Bacon, S. K.: Retropubic Prostatectomy, an Extravesical Technic, J. Urol. **59**:376-384, 1948.

2. Lich, R., Jr.; Grant, O., and Maurer, J. E.: Extravesical Prostatectomy: A Comparison of Retropubic and Perineal Prostatectomy, J. Urol. to be published. Grant, O., and Lich, R., Jr.: Rationale and Results in Retropubic Prostatectomy, Ann. Surg. **127**:1010-1021, 1948. Lich, R., Jr., and Maurer, J. E.: Retropubic Surgery, Kentucky M. J., to be published.

and the empty bladder displaced posteriorly and cephalad. The fat pad over the prostate is displaced laterally to expose the variable vascular endopelvic fascia overlying the prostate. If the veins are prominent, they are individually doubly ligated and severed. If the endopelvic veins are not large, they are disregarded and dealt with individually when bleeding ensues after incision of the prostatic capsule. It has been our practice to introduce a subcapsular suture at the apex of the gland, coursing through the anterior surface of the capsule, to diminish bleeding from the capsular veins. We think that this step is a valuable adjunct.

The prostatic capsule is incised transversely approximately 1.5 cm. distal to the vesicoprostatic junction. The length of the incision is dependent on the size of the prostatic adenoma and is great enough to facilitate an atraumatic enucleation. All layers of the capsule are divided with a single stroke of the knife, and the bulging adenoma can be seen in the opening of the capsular wound. Bleeding from capsular veins at this point may be brisk, but adequate visualization is easily provided by the use of suction. The individual veins are clamped and sutured for positive hemostasis. Mr. Millin employs electrocoagulation for bleeding vessels; however, we have not experienced similarly satisfactory hemostasis. It is to be recalled that these prostatic channels are large caliber veins which have a sparsity of muscle fiber. This may defeat the usual effectiveness of electrocoagulation.

After capsular hemostasis has been accomplished, the prostatic adenoma is separated from the false capsule with scissors point dissection throughout its entire anterolateral circumference, and before the gland is delivered into the retropubic space the posterior urethra is severed with scissors at the apex of the adenoma. When the gland is delivered from the capsule, it is elevated as much as possible in order to visualize its attachment to the vesical neck. The prostate is now attached to the bladder by only a mucosal cuff, and this is cut across. The adenoma is removed, and one can, for the first time, get a glimpse of the bladder cavity through the vesical neck. This entire procedure has been extravesical in both the approach and the enucleation of the adenoma.

The prostatic arteries at the prostatovesical junction are sought and ligated with a figure of eight suture. These arteries normally enter the prostatic capsule at its junction with the bladder at the positions of 5 and 7 o'clock. The vesical neck is then inspected for small bleeding vessels, which are lightly fulgurated. After the vesical neck is free of bleeding points, a catheter is introduced through the urethra; it traverses the prostatic fossa and enters the bladder through the vesical neck.

After the catheter has been introduced, the prostatic capsule is closed with a continuous suture of no. 1 chromic surgical gut including

all layers of the capsule. This suture must be started and terminated well beyond the angles of the capsular wound in order to control all postoperative capsular ooze.

A small drain is left in the space of Retzius; the abdominal wound is closed in layers, and the skin is approximated. Vesical drainage is accomplished by use of the urethral catheter alone. A bilateral vasectomy is done to prevent postoperative epididymitis.

The wound drain is removed on the second postoperative day, and the urethral catheter is removed on the fourth day after operation. The urine will usually be completely clear in twelve to eighteen hours.

We have tabulated herewith a résumé of our first 221 cases of retropubic prostatectomy, which are compared with 500 cases of other open surgical methods of prostatectomy, the majority of which were perineal prostatectomies performed by the late Dr. Owsley Grant

TABLE 1.—*Comparison of Results of Retropubic Prostatectomy and Open Surgical Prostatectomies*

Procedure	No. of Cases	Average Age, Yr.	Hospital Period		Catheter Period, Days	Mortality, %
			Total, Days	Postoperative, Days		
Retropubic prostatectomy.....	221	68.3	17.1	13.1	6.2	3.2
Open surgical prostatectomies.....	500	67.1	31.0	21.8	11.6	3.9

(table 1). It can be seen at a glance that the results are comparable, as might well be expected, since both procedures are extravesical methods of prostatectomy. It is to be noted further that some of the apparent improved figures in the retropubic group could well be occasioned by the fact that antibiotics and sulfonamides were available.

The mortality of 3.2 per cent in the retropubic group was accounted for by 7 patients, all of whom died within fourteen days postoperatively. One died on the fifth day of acute coronary thrombosis; another, 78 years of age, had an uncontrollable cardiac decompensation and bronchopneumonia and died in cardiac failure on the thirteenth day after operation. A man of 66 years died of an overwhelming perivesical infection which had presumably been present, though undiagnosed, preoperatively. He is considered as an ill chosen subject for prostatectomy. The patient would not tolerate either urethral or cystotomy drainage, since both had been used in an attempt to avert operation. The remaining four patients, of 71, 69, 77 and 59 years, died on the seventh, eleventh, thirteenth and sixth days postoperatively of bronchopneumonia, cardiac failure, uremia and an infarct, respectively. The surgical complications which prolonged hospitalization in the series of retropubic prostatectomies are noted in table 2.

Suprapubic fistula occurred in 2 patients. The first had severe diabetes and presented an infection of the wound and a most difficult problem in wound healing; the duration of the fistula was twenty-one days. The subsequent course of the patient has been excellent. The other patient had a huge, narrow-mouthed diverticulum which could not be resected because of the patient's generally poor state. The fistula healed on the twenty-seventh postoperative day.

Infection of the wound was recorded in any case in which there was induration of the wound and possibly some drainage causing the patient to be maintained in the hospital beyond the usually anticipated day of discharge. The longest period of hospitalization in this group was eighteen days.

Secondary hemorrhage from the prostatic bed occurred in 4 patients. In 2 of the group this condition developed during the period of hospitalization, and it was thought that the hemorrhage was due to bleeding from

TABLE 2.—*Surgical Complications*

Complication	No. of Cases	Incidence, %
Suprapubic fistula, temporary	2	0.9
Wound infection	11	4.9
Secondary hemorrhage from the prostatic bed	4	1.8
Osteitis pubis	2	0.9

the prostatic arteries, which had not been ligated. In both instances the bleeding was controlled by endoscopic methods employing electrocoagulation. In the remaining 2 patients the hemorrhages developed after the seventh postoperative day and were controlled by electrofulguration cystoscopically and a Foley catheter. Secondary hemorrhage from the prostatic bed is a hazard of prostatectomy from which no method described thus far has been immune.

There were 2 instances of osteitis pubis, both of which continued for approximately six months. One occurred in a hugely obese diabetic patient, whose convalesence was delayed by poor healing of the wound. The other patient's convalescence was uneventful until the third week postoperatively. From statements in the literature regarding this operation, the appearance of osteitis pubis seems to have been all too frequent, and this fact constitutes certainly a most valid criticism of the operation. It is to be remembered, however, that the syndrome may well not have been so clearly recognized in the past and many instances may have gone undiagnosed, and thus unreported, after other methods of prostatectomy. We have seen 1 instance following perineal prosta-

tectomy, and recently Rosenberg and Vest [3] reported 2 instances following transurethral resection.

We have used this surgical route to deal with lesions of the vesical neck and posterior urethra in infants and children. These lesions in the past have been approached either transvesically or transurethrally, and neither method has proved entirely satisfactory in our hands. The transvesical approach characteristically lacks adequate visualization and positive hemostasis in case of lesions of the vesical neck. The transurethral approach has certain imposed mechanical limitations, particularly in infants. We are aware of the apparent satisfactory use of these two approaches in some clinics, but our experience has not been entirely without dissatisfaction.

We approach the prostate gland in precisely the same manner as the adenoma is approached, but instead of using a transverse capsular incision, we employ a longitudinal incision which extends from the apex of the gland to the prostatovesical junction. At the superior angle of the incision the lateral branches of the prostatic venous plexus are divided, and these vessels are ligated with a single suture on each side of the incision. These sutures are left long to act as tractors, and when lateral tension is exerted the entire posterior urethra and vesical neck are adequately exposed for visualization and palpation. We mention palpation particularly, since in 2 instances in which the obstruction of the vesical neck appeared visually to be relieved, we palpated some dense underlying tissue. This was removed, and the vesical neck could then be visualized and shown by palpation to be free of any obstructing tissue.

After removal of the tissue about the vesical neck, the bleeding points which occur at approximately 5 and 7 o'clock are ligated with a suture of fine surgical gut and immediately the wound is dry. The prostatic capsule is approximated with a running suture of fine chromic surgical gut after a catheter of small caliber has been introduced into the bladder per urethram. The abdominal wound is closed in layers, and a drain is left in place for two days. The catheter is removed on the fourth day, and voiding in these children is spontaneous and uncomplicated.

We have now treated 4 such children, from 3 months to 9 years of age, with excellent results. When the upper urinary tract was uninfected preoperatively, the urine was free of any cellular elements within eighteen days postoperatively. In only 1 case, that of a 3 month old child, did a suprapubic fistula occur, and it closed spontaneously after the catheter was reinserted for a four day period. We have followed 1 of these children for more than a year postoperatively and

3. Rosenberg, M. L., and Vest, S. A.: Osteitis Pubis, J. Urol. **60**:767-775, 1948.

another for a six month period; the remaining 2 have been observed three and two months respectively. When an elevated nonprotein nitrogen level was stabilized preoperatively by catheter drainage, the level obtained did not change after operation. Morbidity has been surprisingly insignificant.

It can be seen from the statements that Mr. Millin's rediscovery of the retropubic, or anterior extravesical, approach to the prostate offers more than just another means of prostatectomy.

SUMMARY

The retropubic, or anterior extravesical, approach to the prostate gland is discussed and a series of 221 cases presented in which this method of prostatectomy was used to remove a benign prostatic hyperplasia. In addition, the value of this route in treating lesions of the vesical neck and urethra in infants and children is pointed out. A series of 4 cases is presented which demonstrated a most gratifying result in every instance. We report on this numerically inadequate group of children to suggest additional trial by others in an attempt to secure accurate evaluation. The real contribution is that for the first time a simple, effective extravesical approach to the prostate has been demonstrated which affords the simplicity of the suprapubic prostatectomy but, in contrast, is firmly established on sound surgical principles.

SURGICAL MANAGEMENT OF RESPIRATORY EMERGENCIES DURING THE FIRST FEW WEEKS OF LIFE

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SINCE respiratory embarrassment in the newborn is a frequently encountered condition which may merit consideration and treatment from a surgical standpoint, it is our purpose to discuss 3 illustrative instances in which radical surgical measures were necessary in the treatment of infants whose dyspnea and cyanosis noted at birth failed to improve. Mitchell-Nelson's Textbook of Pediatrics [1] states that almost one half of the deaths of newborn infants are due to respiratory failure.

Morgan and Brown [2] listed nine accidents during labor which produced cyanosis of the newborn. Only one of these, aspiration of amniotic fluid, directly concerns the surgeon. This aspiration may cause bronchial obstruction with attendant emphysema or atelectasis, for which surgical treatment may be necessary. Since atelectasis is always present at birth, the degree and rate of expansion of the lungs in the newly born child may be significant.

Wasson [3] made roentgenograms of the chest at frequent intervals after birth to determine the natural history of aeration in the lung of the newborn infant. He found that in some infants whose delivery was easy the lungs were completely expanded in five minutes. After more prolonged deliveries, complete expansion of the lungs was noted at longer intervals after birth, in some cases being delayed up to two weeks. In some instances, entire lobes remained atelectatic; in others there were scattered areas of lobular atelectasis. The lower lobes were

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From the Department of Surgery of the University of Buffalo School of Medicine and the Children's Hospital.

1. Nelson, W. E.: Textbook of Pediatrics, Philadelphia, W. B. Saunders Company, 1946, p. 235.

2. Morgan, E. A., and Brown, A.: Cyanosis of the New-Born, J. A. M. A. **105**:1085 (Oct. 5) 1935.

3. Wasson, W. W.: A Roentgenographic Study of the Infant Chest As Seen at Birth, J. A. M. A. **83**:1240 (Oct. 18) 1924.

usually the last to expand. Clinical symptoms were or were not present, depending on the degree of atelectasis. It is important to keep the natal history in mind when considering a case of respiratory distress with signs and symptoms of pulmonary atelectasis.

Central disturbances caused by intracranial lesions with consequent poor pulmonary ventilation must be considered in cyanosis of the newborn. The premature infant may have marked underdevelopment of the bronchial tree as well as the thorax, which is evidenced by areas of the lung which do not become filled with air. Even agenesis of an entire lung has been reported.

Congenital diaphragmatic hernia is a cause of respiratory distress due to increased pressure on the lungs and mediastinum. This condition, which necessitates immediate surgical intervention in the newborn, has been relatively frequent in our experience and is not reported in detail. The subject has been adequately covered by other authors: Harrington,[4] Ladd,[5] Gross[6] and Donovan.[7] We are strongly of the opinion that reduction of the hernia and early repair of the defect are extremely important and prefer to operate on these infants within the first forty-eight hours of life, unless contraindications present themselves. For the same reason, tracheoesophageal fistula is not discussed but is included as one of the surgical emergencies encountered in dealing with the respiratory system. Eventration of the diaphragm has been reported and deserves a place in these considerations.[8]

Since overdistention of a lobe or lobes combined with mediastinal displacement during the first few weeks of life can cause what constitutes a surgical emergency, it is our desire to review the recorded cases and report in more or less detail the successful results and to discuss briefly the underlying conditions.

Case 1.—A white boy, aged 11 weeks, was admitted to Children's Hospital Dec. 23, 1947. The birth history, obtained from another hospital (which is outside Buffalo), reveals an extremely difficult delivery, after which the child showed bruises over almost his entire body and one eye was closed from ecchymosis. The onset of breathing was slow, and mechanical resuscitation was necessary. Penicillin was administered because of elevation of temperature to 101 F. When the child

4. Harrington, S. W.: Surgical Treatment of the More Common Types of Diaphragmatic Hernia; Esophageal Hiatus, Traumatic, Pleuroperitoneal Hiatus, Congenital Absence and Foramen of Morgagni: Report of Four Hundred and Four Cases, Ann. Surg. **122**:546, 1945.

5. Ladd, W. E., and Gross, R. E.: Congenital Diaphragmatic Hernia, New England J. Med. **223**:917, 1940.

6. Gross, R. E.: Congenital Hernia of the Diaphragm, Am. J. Dis. Child. **71**:579, 1946.

7. Donovan, E. J.: Congenital Diaphragmatic Hernia, Ann. Surg. **108**:374, 1938.

8. Bisgard, J. D.: Congenital Eventration of the Diaphragm, J. Thoracic Surg. **16**:484, 1947.

was taken home from the hospital after delivery, he appeared normal with the exception that he breathed with difficulty and retracted both ribs and abdomen with each respiratory effort. Six weeks after birth, a wheeze developed, which continued and became progressively worse. Approximately during the seventh week, he suffered an acute episode, at which time there was severe respiratory difficulty with profuse sweats and the infant seemed to gasp for air. The parents thought that he was dying. After medical treatment administered by the local physician, the wheeze disappeared, only to return again. There was only an insignificant cough and no cyanosis. On the day before admission, he had more trouble breathing. On admission, the child was in considerable distress; respirations were labored, wheezy and associated with substernal retraction. He was not cyanotic but assumed a dusky hue when he cried.

Physical examination revealed nothing of significance except for the thorax. There were rapid wheezing respirations with both phases shortened. Substernal retraction was noted. There was very little expansion of the thoracic cage. Breath sounds were decreased throughout the entire left side of the chest and increased in the lower right pulmonary field; they were diminished in the right upper field Posteriorly, rales were heard at the apex of the right lung. Percussion revealed hyperresonance at the base and dulness at the apex of the right lung. Findings were unchanged over the left side. The cardiac dulness was detected in the right side of the chest. The tones were distant and not well heard. They were most distinct between the right midclavicular line and the sternum in the fourth interspace. The child was afebrile, with respirations averaging 32 per minute. He was in oxygen much of the time preoperatively and showed evidence of slight cyanosis when crying or moving about. His appearance was listless, and his feedings were taken poorly. Determinations of the hemoglobin level showed an average value of 12 Gm., and the white blood cells ranged from 6,550 to 18,400 preoperatively, with 46 per cent filamented cells, 8 per cent band cells, 42 per cent lymphocytes and 4 per cent eosinophils. Otherwise, the results of laboratory studies were of no significance. Bronchoscopic examination was done on December 26. A 3.5 mm. bronchoscope was easily passed. The trachea, both main bronchi and the carina were normal. There was no evidence of inflammation. A thin white mucus was seen, which was cultured. A growth was obtained which was reported as a gram-negative bacillus identified as Escherichia coli. The orifice of the right main bronchus could be seen, and it appeared normal. The orifice of the bronchus to the upper lobe of the left lung could not be seen because there was a slight bulge at this area. An impression was gained that mucosa was everted at the opening of the upper lobe. It was felt that this could be compatible with a distended upper lobe and that if any obstruction in the bronchus to the upper lobe of the left lung was present it was beyond the point of visualization.

Operation (L. J. L.).—When the infant was 14 weeks of age, under intratracheal anesthesia administered through a no. 1 Magill tube, a posterolateral incision was made over the left side of the chest. The thorax was opened through the fifth interspace, and on opening of the pleura the lung bulged through the incision, without positive pressure applied by the anesthetist. On examination of the left side of the thorax, a large mediastinal hernia, a greatly overdistended upper lobe and a collapsed lower lobe were observed. The upper lobe occupied practically the entire side, and the lower lobe was merely a small, shrunken mass against the mediastinum. The upper lobe was pink; the pleural surface was tense and smooth. It appeared to be definitely emphysematous throughout. It was impressive to note that the vessels to the upper lobe were smaller and more collapsed than normal. The lobe did not deflate after removal. There were no

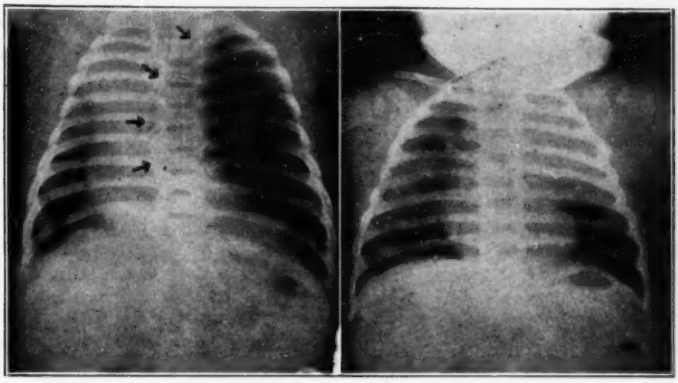

Fig. 1 (case 1).—Preoperative and postoperative roentgenograms of an infant with hypertrophic emphysema.

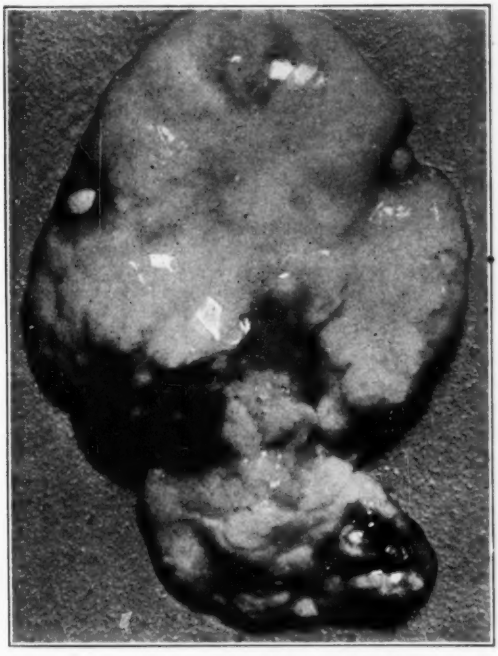

Fig. 2 (case 1).—Resected upper lobe of left lung, showing marked distention.

cystic areas visible. The upper lobe was removed after individual ligation of the vessels with silk. The bronchus was amputated close to its origin, about 0.5 cm. beyond its division from the main bronchus, and the stump was closed over with interrupted silk sutures. Moderate positive pressure was applied through the intratracheal tube, and there was no leakage of air from the bronchial stump. The lower lobe seemed to aerate without any difficulty. A no. 12 F. de Pezzar catheter was placed in the posterior portion of the wound, which was closed in layers with chromic surgical gut. Fluids and whole blood were introduced through a cutdown in the ankle vein during the operation.

The postoperative period was without untoward incidents. Feedings were resumed on the afternoon of operation and continued without interruption. Administration of oxygen was maintained for twenty-four hours and was not necessary thereafter. The catheter was removed from the thorax at the end of thirty hours, with a total drainage of 220 cc. of clear, amber-colored fluid. A roentgenogram taken with a portable machine on the afternoon of operation showed the lower lobe of the left lung to be reexpanded. The mediastinum was central, and there was an area of density in the upper half of the left side of the chest. The right lung was aerated in all lobes.

Pathologic Report.—Various sections taken from the extirpated lobe showed largely alveolar emphysema with some blebs of considerable size, exceeding that of the lumens of all bronchi contained in this section. Although some of the bronchi were dilated, their lumens were free of secretion. There was some edema surrounding the pulmonary arteries in the hilar area, extending through the interlobular fissures into the pleura. Numerous distended air sacs alternated with distinctly atelectatic areas. Some intervening lobules contained very thin watery material (edema) with but few desquamated macrophages. Some smaller caliber bronchi draining the atelectatic areas were also completely collapsed.

Other sections showed a largely similar picture, with prominently distended bronchi, air sacs and alveoli and with some edema intervening between the alveoli which were not atelectatic. In other sections, again taken from the perihilar area, the atelectasis was considerable with the bronchi entirely collapsed, while nearby bronchi, only a few millimeters away, as well as part of the adjacent alveolar tissue appeared markedly distended. Part of the subpleural lobules, however, appeared entirely collapsed. In this section edema, involving again the interlobular fissures, was pronounced. The elastic membranes in the arteries and bronchi throughout were well preserved.

Finally, in several lobules near the hilus the atelectatic alveoli were almost entirely filled with the previously mentioned debris containing macrophages but no other cellular exudate. The pulmonary arteries surrounding bronchi of first order at the hilus appeared very prominently separated from the partly atelectatic pulmonary tissues by periadventitial edema.

Postoperative Course.—Follow-up examination six months after operation revealed breath sounds normal throughout both sides of the chest and the heart in normal position. The parents stated that since discharge from the hospital the child had breathed easily at all times, there had been no struggle and, whereas prior to operation he used to "shake the crib with his efforts," respirations were now perfectly normal. There had been a steady gain in weight. Roentgen examination showed all the remaining lobes to be clear, well aerated and normal in position. The lower lobe of left lung had not completely filled the hemithorax but had progressively increased in size to occupy the position of the resected upper lobe. The weight was 23 pounds (10.4 Kg.).

A survey of the literature and textbooks on pathology fails to reveal a classification which exactly fits this particular type of lesion unless it is assumed that a bronchial obstruction existed in the upper lobe of the left lung.

Jackson[9] discussed thick secretions as the cause of bronchial obstruction. In our case there was no evidence of bronchiectasis or cystic disease. Royes,[10] in a case report on an adult, entitled "Localized Hypertrophic Emphysema," described emphysema of the middle lobe due to a flap of mucous membrane which included five eighths of the lumen of the bronchus. He assumed that this mucosal flap acted as a valve and gave rise to the localized hypertrophic emphysema. There were no cavernous areas found.

Gordon[11] referred to a flap of mucous membrane lodging in a bronchus in such a manner that a check valve mechanism occurred and discussed the mechanism of hypertrophic pulmonary emphysema. He mentioned that the condition is reputed to be without known cause but that there are a multitude of suggestive theories of origin, which he discussed and largely discredited as causative agents. None of them would in any way apply to the case herein reported unless it is assumed that the bronchial mucosa was redundant. Gordon retained two theories as having, in his opinion, some validity. These are (*a*) the theory of compensatory distention and (*b*) the theory of obstruction; he commented that the theory of obstruction is a subdivision of the theory of compensatory distention.

Caffey,[12] in a paper in which he discussed regional obstructive pulmonary emphysema in infants and children, reported 7 cases, in each of which there was associated respiratory infection. The youngest patient was 3 months of age. Cystic dilatation, which was universally noted on the roentgenograms of the chest, was explained on the basis of emphysema. The lesions were not thought to be consistent with pulmonary abscess or congenital cystic disease of the lungs. In all these patients the return to normal was observed following nonoperative treatment. This author stated that if the bronchial obstruction is of

9. (*a*) Jackson, C.; Spencer, W. H., and Manges, W. F.: The Diagnosis and Localization of Non-Opaque Foreign Bodies in the Bronchi, Am. J. Roentgenol. **7**:277, 1920. (*b*) Jackson, C.: The Mechanism of Physical Signs with Especial Reference to Foreign Bodies in the Bronchi, Am. J. M. Sc. **165**:313, 1923. (*c*) Jackson, C.: Bronchoscopy: Past, Present and Future, New England J. Med. **199**:759, 1928.

10. Royes, K.: Localized Hypertrophic Emphysema, Brit. M. J. **2**:659, 1938.

11. Gordon, I.: The Mechanism of Hypertrophic Pulmonary Emphysema, Dis. of Chest **10**:180, 1944.

12. Caffey, J.: Regional Obstructive Emphysema in Infants and in Children, Am. J. Dis. Child. **60**:596, 1940.

Fig. 3 (case 1).—Photomicrographs of resected emphysematous lobe.

Figure 3 continued.

the check valve type, so that the inflow of air is free during inspiration, the escape during expiration is obstructed and accumulative alveolar distention occurs in the distal segment of the lung.

Paine [13] and others have shown experimentally that emphysematous changes followed placement of check valve obstructions in the trachea of dogs. Rubin,[14] in his textbook, mentioned that since the distended lungs are in contact with the chest wall forcible compression is required in an effort to deflate them in order to permit an interchange of gases and stated that all the accessory muscles of respiration have to be brought into action. This could explain the abnormal breathing that this infant exhibited.

Snow and Cassasa [15] reviewed roentgenograms of 70 infants under 1 year of age with a clinical diagnosis of pneumonia. It was their observation that in almost every case there was some degree of emphysema, with extreme degrees in many cases, particularly in infants under 6 months of age. Displacement and rotation of the heart with depression of the diaphragm was noted. They emphasized the point that severe tension was necessary for displacement of the mediastinum. These observers felt that the changes in aeration of the lung were caused by valvular effects in the bronchial tree which were the result of inflammatory reactions and secretions. Four roentgenograms reproduced in their article illustrate conditions closely similar to those in the case herein described.

McNeil and co-workers [16] stated in an article dealing with pneumonia in children that a degree of acute vesicular emphysema may be present in either lobar pneumonia or bronchopneumonia.

Maxwell [17] discussed the subject of localized emphysema from the standpoint of incomplete bronchial obstruction and reported 6 cases. One of the patients was a 2½ year old child whose left lung was in such a state of extreme emphysema that spontaneous pneumothorax was suspected. There was sudden change in physical signs before bronchoscopy could be accomplished, and within a few hours the clinical signs and symptoms returned to normal. This was confirmed by roentgenograms. Mucus was assumed to be the causative agent.

13. Paine, J. R.: Studies in the Experimental Production of Pulmonary Emphysema, J. Thoracic Surg. **10**:150, 1940.

14. Rubin, M., and Rubin E.: Diseases of the Chest, Philadelphia, W. B. Saunders Company, 1947, p. 355.

15. Snow, W., and Cassasa, C. S.: Obstructive Emphysema and Atelectasis in Acute Respiratory Diseases of Infants, Am. J. Roentgenol. **37**:220, 1937.

16. McNeil, C.; McGregor, A. R., and Alexander, W. A.: Studies of Pneumonia in Childhood, Arch. Dis Child. **4**:83, 1929.

17. Maxwell, J.: Localized Emphysema As a Sign of Incomplete Bronchial Obstruction, Brit. M. J. **1**:520, 1940.

Salmon, Forbes and Davenport [18] studied the autopsy findings in 6 infants dying shortly after birth with pneumothorax and pulmonary emphysema. There was no evidence of bronchial obstruction in these lungs. They examined the lung under the dissecting microscope and found a honeycomb appearance due to extensive interstitial pulmonary emphysema. Excessive pulmonary ventilation incident to difficult birth and artificial respiration caused rupture of the alveoli, in their opinion. The air liberated in this fashion dissects along the pulmonary vessels and on reaching the visceral pleura may rupture through and even cause a pneumothorax. The air remaining in the interstitial pulmonary tissues may cause a very inelastic lung which collapses but little during the respiratory cycle. The authors applied the general term "air block" to this condition, in which air reaches the interstitial pulmonary tissue and may spread to the pleural cavity, to the mediastinum, to the retroperitoneal space and even over into the other lung. This affords a plausible explanation for extensive degrees of emphysema not associated with bronchial obstruction.

The etiologic factor in our case has not been determined. Bronchoscopic examination suggested some bulging in the location of the bronchus to the upper lobe. It is not clear whether this was obstructive in nature and whether the respiratory difficulties at the time of birth, which required rather energetic efforts to overcome, were significant. There was evidence of pulmonary infection both immediately after birth and at 7 weeks of age. Also a wheeze was noted by the parents. Examination at the time of operation failed to reveal any obstructive lesion, and careful dissection of the gross specimen and further microscopic investigation failed to show any obstructive type of lesion. Although evidence of bronchial obstruction was not positive, it was at least highly suggestive, but we are at a loss to discover the type or location. There was no evidence of pneumonia in the resected lobe. This infant was operated on with the probable diagnosis of cystic disease.

The next case, which followed a somewhat similar course, proved to have an extrapulmonary lesion as a causative factor. Immediate operation established the diagnosis and resulted in complete relief of symptoms.

CASE 2.—A. B., a white boy, was delivered normally at term and weighed 8 pounds (3,630 Gm.). Shortly after birth he was observed to have rapid, labored respirations and cyanosis. The child was placed in oxygen. Frequent suctioning of the pharynx was necessary to remove mucoid secretions. The temperature varied from 99.2 to 101.4 F.; respirations, from 80 to 110, and pulse rate, from 110 to 140. Examination of the chest revealed marked suppression of the breath

18. Salmon, G. W.; Forbes, G. B., and Davenport, H.: Air Block in the New Born Infant, J. Pediat. **30**:260, 1947.

sounds on the right, with dulness to percussion throughout. The roentgenogram showed atelectasis of the upper and lower lobes of the right lung and emphysema of the middle lobe.

Bronchoscopy showed the right main bronchus to be nearly occluded in its lower portion by a swollen membrane and thick mucus. The mucus was removed and a dilating forceps introduced and expanded. Improvement of breathing followed. The child was able to be out of oxygen without cyanosis. The temperature returned to normal. The upper lobe expanded, and the middle lobe became less emphysematous, but the lower lobe remained atelactatic on roentgen examination. On the tenth day after birth the general condition seemed good, and the formula was being taken well; hence the child was discharged from the hospital.

Three weeks later, the child was readmitted because of cyanosis and labored breathing. The clinical impression was of a pleural effusion on the right side with mediastinal shift. This impression was confirmed by roentgen study. The temperature remained normal. On examination the blood and urine were normal. The child was again placed in oxygen.

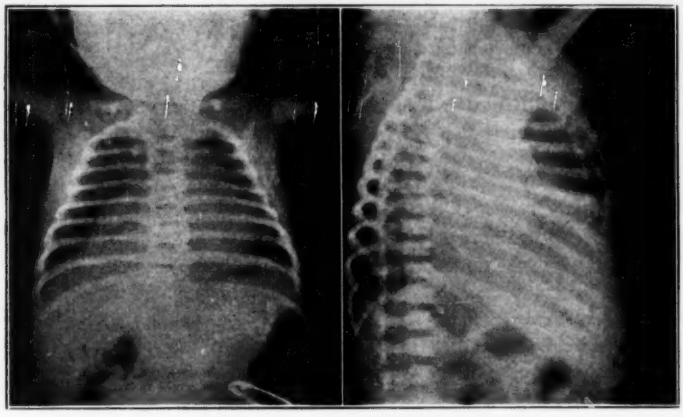

Fig. 4 (case 2).—Anteroposterior and lateral roentgenograms taken shortly after birth of an infant with gastrogenic cyst.

During the next two weeks, six thoracenteses were performed on the right posterior part of the chest, fluid varying from 30 to 80 cc. being removed. This resulted in marked improvement in the child's condition. The fluid was clear and straw colored. It contained 350 to 500 polymorphonuclears, chiefly lymphocytes, per cubic centimeter. The total protein content varied from 0.6 to 0.7 Gm. per hundred cubic centimeters. No organisms were recovered on culture. Repeated roentgen examination of the child by now showed a marked change. The upper two thirds of the right side of the chest showed the presence of a small amount of air, with slight pleural thickening. A large pocket measuring 6 by 5 by 4 cm. with a wall 1 cm. thick was found in the lower posterior half of the right side of the thorax. This pocket had a fluid level.

A diagnosis of congenital pulmonary cyst was made, and the child operated on (W. L. B.) at the end of the seventh week of life, under cyclopropane anesthesia

administered through an endotracheal tube. The parietal pleura on the right was found to be thickened and dull in appearance. The visceral pleura, which was also thickened, was everywhere adherent with fibrinous adhesions which were easily separated bluntly. A small pocket containing shaggy fibrinous exudate and straw-colored fluid was found in the right costophrenic sinus. As they approached the posterior thoracic gutter, the two pleural layers were so densely adherent that they were not separated for fear of tearing the lung. At this point the dissection was begun in the retropleural space. A thick cyst wall was encountered, which was freed from the pleura anteriorly and the endothoracic fascia posteriorly. As the procedure developed, it became obvious that the wall was made up of smooth muscle, the appearance being exactly like that of stomach. An anomalous vessel the size of a match supplied it from the aorta, as did three branches from intercostal arteries. As the dissection progressed, the cyst was found to lie contiguous with the lower esophagus for a distance of 4 cm. and to send a projection to the cardia of the stomach. It measured 12 by 7 by 6 cm., and when it was opened

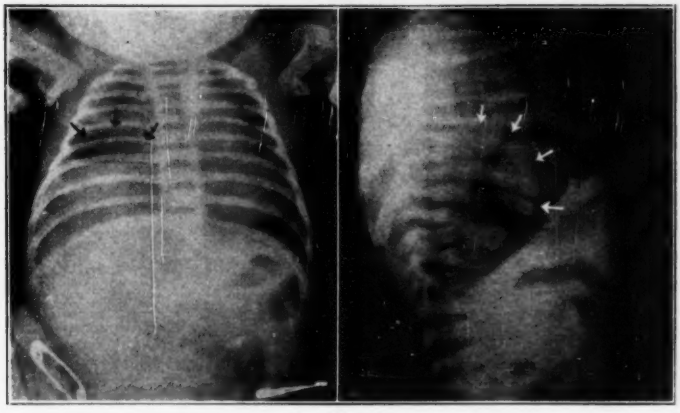

Fig. 5 (case *2*).—Anteroposterior and lateral roentgenograms of infant with gastrogenic cyst taken immediately before operation.

typical gastric rugae were seen, together with clear fluid. The lung was reexpanded, and the thoracic cavity was closed without drainage. A roentgenogram taken at the conclusion of the operation showed the lung to be completely reexpanded.

The postoperative course was entirely uneventful. The child left the hospital two weeks later, in excellent condition, with all lobes of the lung reexpanded. Section of the cyst wall showed all layers—mucosa, submucosa and the outer muscular layers—to correspond exactly to layers of the normal stomach. One small tubelike projection showed a mucosa which resembled a jejunal pattern with well preserved villi. The histologic diagnosis was gastrogenic cyst.

This case was important because of its changing manifestations and the speculation that was aroused as to the exact cause of the respiratory distress. Roentgenograms taken shortly after birth revealed a homogeneous density over the right side of the chest that was inter-

preted as atelectasis. Later films were suggestive of varying degrees of bronchial obstruction with atelectasis of the upper and lower lobes of the right lung, accompanied with emphysema of the middle lobe. Bronchoscopic examination did not reveal the cause of the obstruction, but the increased drainage which followed appeared to result in better aeration of the lung and improvement in the infant's condition. Again difficulty in breathing and cyanosis occurred. This time the roentgenogram suggested a pleural effusion. Thoracentesis apparently established this impression as true but was followed by a rapid reaccumulation of the fluid. The diagnosis was finally established on the basis of a roentgenogram taken after one of the aspirations of the chest. The fluid in the cyst cavity had probably been aspirated on this occasion,

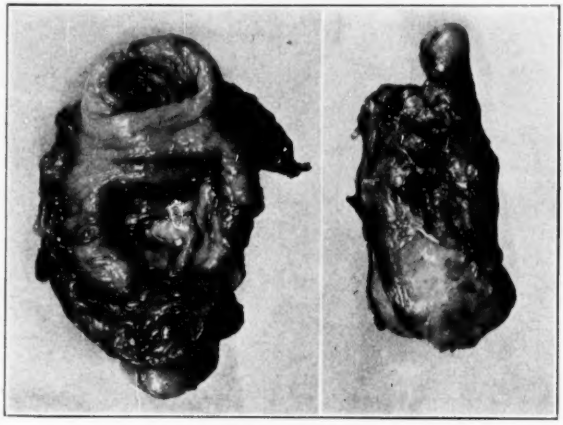

Fig. 6 (case 2).—Resected gastrogenic cyst.

since the film showed a typical cyst structure. This was interpreted as being a pulmonary cyst. Thus the protean nature of the cyst prevented an exact diagnosis until the thoracotomy was done.

Intrathoracic cysts of gastric origin were formerly considered rarities. Now, with the increasing frequency and safety of surgical procedures within the thoracic cavity, reports are more numerous. A backward look over the literature will necessarily fail to give completely accurate information because of terminology. Many mediastinal cysts have linings which indicate their origin from multiple sources. Combinations of bronchial, esophageal, gastric and enteric types of mucosal linings are found. Cysts with a lining of gastric mucosa are usually larger and produce severe symptoms, as found in this case. Cysts of

esophageal origin tend to be smaller and are more compatible with life.

Olenik and Tendatnick [19] have reported a cyst of mixed gastric and intestinal epithelium in a 9 day old boy and have added an extensive survey of the literature up until 1947. They found 74 cases of intrathoracic cysts of foregut origin. In 27 of the collected cases the cysts were of gastric or intestinal origin. It is significant that the oldest of these 27 patients was aged 3 years and 9 months. This implies that these cysts exert an exceedingly dangerous influence on the child. Surgical consideration cannot fail to take this into account. Operative intervention was undertaken in 16 of these cases, with a successful outcome in 8.

Since that report, Davis and Salkin [20] have found 26 cases reported in the literature, with surgical treatment in 17, which was successful in 10. Adding the cases with successful outcome reported by these groups of authors to that of Lindquist and Wulff,[21] a case recently reported by Ehler [22] and the case here described, the total is 21 with 14 recoveries. Cases in older age groups are now being reported; Dickson, Clagett and McDonald [23] operated on a girl, aged 10; Davis and Salkin,[20] on a girl, aged 14, and Schwarz and Williams,[24] on a man, aged 23.

The symptoms of these cysts are those of pressure in the mediastinum. Cough, cyanosis, dyspnea and regurgitation of food result. More specifically, the pressure may be on the bronchus, in which case it is followed by atelectasis, obstructive emphysema and occasionally hemoptysis. If the child lives long enough, recurrent pneumonia and bronchiectasis occur. Hematemesis has resulted from pressure on the esophagus.[25] Peptic ulceration of the gastric cyst with penetration into the lung is a rare finding.[26]

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19. Olenik, J. L., and Tendatnick, J. W.: Congenital Mediastinal Cysts of Foregut Origin, Am. J. Dis Child. **71**:466, 1947.

20. Davis, E. W., and Salkin, D.: Intrathoracic Gastric Cysts, J. A. M. A. **135**:218, 1947.

21. Lindquist, N., and Wulff, H. B.: Mediastinal Enterocystoma, J. Thoracic Surg. **16**:468, 1947.

22. Ehler, A., and Atwell, S.: Gastric Cyst of the Mediastinum, J. Thoracic Surg. **17**:809, 1948.

23. Dickson, J. A.; Clagett, O. T., and MacDonald, J. R.: Intrathoracic Gastric Cyst, J. Thoracic Surg. **15**:318, 1946.

24. Schwarz, H., and Williams, C. S.: Thoracic Gastric Cysts, J. Thoracic Surg. **12**:117, 1943.

25. Ladd, W. F., and Scott, H. W.: Esophageal Duplication or Mediastinal Cysts of Enteric Origin, Surgery **16**:815, 1944.

26. Seydl, G. H.: Eine kongenitale Magenwandcyste im Mediastinalraum mit in die Lunge perforiertem Ulcus pepticum, Frankfurt. Ztschr. f. Path. **52**:346, 1938.

If the diagnosis can be made otherwise, we feel that aspiration of the cyst is dangerous, as it may lead to infection. Experience seems to point now to the fact that immediate excision of the cyst is the safest course to follow. As Ladd and Scott have pointed out, marsupialization may be necessary in certain cysts that have a muscular wall in common with the esophagus. Later these authors accomplish destruction of the lining of the cyst.

The third case again exemplifies an occasion of the futility of conservative efforts to overcome dyspnea and cyanosis when the underlying condition was congenital cystic disease of the lung.

Case 3.—R. R., a white boy, was delivered normally at term. At first, he had some difficulty in breathing, but oxygen was not necessary. However, the mother

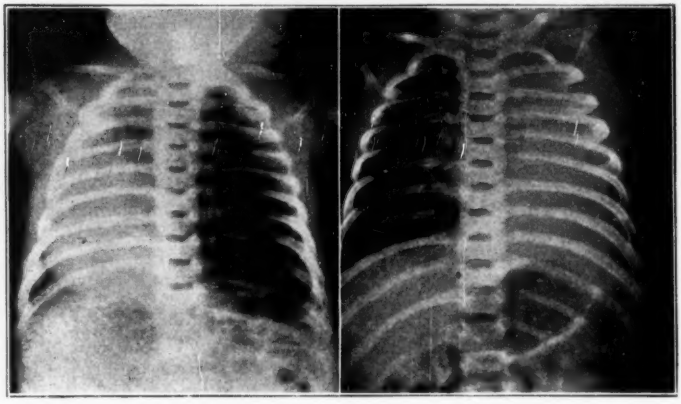

Fig. 7 (case 3).—Preoperative (anteroposterior) and postoperative (anteroposterior) roentgenograms of infant with cystic disease of the left lung.

stated that breathing had never been normal since birth, that the child cried in gasps and turned blue when crying hard. The child was so easily exhausted by any movement that it interfered even with his eating. There were three previous admissions to another hospital, where the child was given oxygen therapy for dyspnea. He was admitted to the Children's Hospital at the age of 7 weeks.

Roentgen examination showed marked emphysema of the entire left lung with large bleb formation, particularly at the base. The heart and mediastinum were shifted to the right. There was increased density of pulmonary tissue on the right consistent with compression atelectasis of the right lung.

Operation was carried out under cyclopropane anesthesia on the day of admission by Dr. J. F. MacManus. When the left pleural cavity was opened, the entire lung was found to contain numerous cysts, particularly the upper lobe, which had been completely replaced by large cysts. The air was removed from the large cysts to facilitate removal, and hilar dissection was carried out, with removal of

the lung. The bronchus was closed with interrupted silk sutures. The mediastinal pleura was closed with interrupted silk sutures and the chest closed without drainage.

The postoperative course was uneventful except for a mild unexplained febrile reaction which began on the sixth postoperative day and lasted three days. The child left the hospital at the end of two weeks in excellent condition and without any difficulty in breathing. The examination of the removed specimen showed the entire lung to contain multiple cysts varying in size from that of a match head to that of a walnut. Sections through the cysts showed a well preserved high columnar epithelial lining resting on a thin mesenchymal membrane attached to a thin layer of smooth musculature. The intervening pulmonary tissue showed pressure atelectasis.

The chief importance of pulmonary cysts relative to this discussion is the tendency of one type to cause a serious degree of respiratory distress. This is the expansile, or balloon, cyst. In Schenck's [27] series of cases collected from the literature, 86 per cent of expansile cysts were found in infants. These cysts are all connected with the bronchial tree, but when the connection is of a tortuous type air may be trapped within them, producing a great increase in size. This expanding lesion within the chest may cause severe displacements in the mediastinal organs as well as pulmonary compression. Cyanosis and rapid, tugging, inefficient respirations from the compression during the first few days or weeks of life demand immediate relief.

The type of relief decided on in the case reported here was pulmonary resection. Four previous instances [28] have come to our attention in which lobectomy or pneumonectomy was performed for this emergency in infants. The results have been uniformly good. Absence of infection and ease of developing the hilus in the infant contribute to the smoothness and speed of the operative procedure. The postoperative events in these reported cases and in our own case indicate that the infants withstand the operation remarkably well.

In 1933, Anspach and Wolman [29] reported a case of a large balloon cyst discovered in infancy and described 5 other cases collected from the literature. All the patients had died. They said that "surgical removal of lung cysts has not been attempted in infants. It is hoped that a

27. Schenck, S. G.: Diagnosis of Congenital Cystic Disease of the Lung, Arch. Int. Med. **60**:1 (July) 1937.

28. Fischer, G. C.; Tropea, F., and Bailey, C. P.: Congenital Pulmonary Cysts, J. Pediat. **23**:219, 1943. Gross, R. E.: Congenital Cystic Lung, Ann. Surg. **123**:229, 1946. Burnell, W. E., and Caswell, H. T.: Lobectomy for Pulmonary Cysts in a Fifteen Day Old Infant with Recovery, Surgery **23**:84, 1948. Chisholm, T. C.: Lobectomy for Pulmonary Cysts in a Five Day Old Infant, personal communication to the authors.

29. Anspach, W. E., and Wolman, I. J.: Large Pulmonary Air Cysts of Infancy, Surg. Gynec. & Obst. **56**:635, 1933.

satisfactory treatment will eventually be devised to prevent high mortality in infants and young children." In their series of cases, repeated thoracentesis failed to prevent death from asphyxia. Even a tube with a one way valve placed into the cyst was unavailing. The use of thoracentesis may be associated with untoward results. Spontaneous pneumothorax with inability to expand the lung may follow. Even a tension pneumothorax can occur.

There is always the danger of infection and the grave results of toxemia from this source in infants. Collapse, necessitating the use of artificial respiration to maintain life, has resulted from thoracentesis. Numerous examples can be found in the literature in which aspiration of the cyst was followed by only momentary or no improvement, the infant dying a few days to weeks later.

In some instances the primitive bud from which the cyst has developed is so separated from the rest of the lung that the cyst alone can be removed by ligating its pedicle. We have encountered such a cyst in an adult. However, most of the time the enucleation of the cyst is not feasible in infants, as the separation of the cyst from the lung involves too much loss of blood. If the infant's condition is very poor on the operating table one can consider marsupialization of the cyst. This procedure leaves an avenue open for subsequent infection and necessitates further surgical measures. A tourniquet ligation of the hilus of the lung or the lobe could be considered if the risk is desperate. Although this is more easily accomplished and followed by better results in infants than in adults, individual ligation should be performed unless the circumstances are most extenuating.

Nonexpansile and fluid-filled cysts have not been discussed. They do not ordinarily constitute an emergency during the first few days of life. However, if they did, pulmonary resection would, in our opinion, provide the safest procedure.

The danger resulting from aspiraion of these cysts must be emphasized. Aspiration may lead to infection or a leak in the cyst wall, causing tension pneumothorax. Either of these eventualities may seriously compromise the infant's chance to get well and cause serious complications. Immediate resection will carry a more favorable prognosis than any temporizing procedure. Souders [30] has commented on the well known propensity of these cysts to interfere with pulmonary function and give rise to recurring episodes of pulmonary infection by their pressure on a bronchus.

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30. Souders, C. R.: The Sequelae of a Balloon Cyst, Lahey Clin. Bull. **5**:249, 1948.

CONCLUSION

It appears that immediate removal of the underlying pathologic cause is the safest measure to relieve the respiratory embarrassment in the types of cases reported.

We feel that nothing is to be gained by delay, since progression of the tension within the lesion and infection are a constant threat to the child's life.

Aspiration of intrathoracic cystic lesions in infants increases the danger from infection or tension pneumothorax.

ADDENDUM.—Since this report was submitted for publication, we have encountered an instance of severe dyspnea in a newborn infant, caused by eventration of the left half of the diaphragm. This was repaired by a transabdominal approach, with reposition of the diaphragm at its normal level and complete clinical recovery.

Dr. Kornel Terplan, pathologist to the Children's Hospital, made the histologic examinations of the tissue in these cases.

SURGICAL MANAGEMENT OF OMPHALOCELE

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AN OMPHALOCELE is a congential anomaly that is occasionally seen. Some authors [1] have estimated the incidence as being 1 in 5,000 births. This ratio means, in itself, that the presence of a true omphalocele is a relatively rare surgical condition. It is probably true that up until the past several decades a number of infants with omphaloceles were allowed to die without surgical intervention or, if an attempt were directed toward surgical correction, it was unsuccessful and the termination was fatal. Even though the number of omphaloceles seen by any one surgeon or by a clinic is relatively small, emphasis should be placed on the correct surgical management of the condition when it does present itself.

Up until the time that Ladd and Gross [2] first published their report of a series of omphaloceles the condition has been designated by a number of terms, which only led to a moderate degree of confusion. Some of these terms are congenital eventration; hernia into the umbilical cord; amniocele or amniotic hernia; funicular hernia of the umbilical cord; exomphalos and, erroneously, umbilical hernia. Ladd and Gross emphasized the use of the term omphalocele as suitable for the condition in an effort to differentiate it from umbilical hernia. This use of a constant term permitted grouping of all the other conditions under a usable and suitable heading. The frequent use of the word "hernia" in so many of these descriptions only led to confusion and a false impression that umbilical hernia and omphalocele were closely allied. At the present, it is well understood that from both an embryologic and an anatomic standpoint the two lesions are entirely different. An umbilical hernia results from an incomplete formation and fusion of normal fascia and muscle layers of the anterior abdominal wall in such a way that a defect is formed at the umbilicus, which after birth may become larger.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

From the University of Louisville School of Medicine and the Surgical Departments of Louisville General Hospital.

1. Margulies, L.: Omphalocele (Amniocele), Am. J. Obst. & Gynec. **49**:695-699 (May) 1945.

2. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1941.

It is covered by peritoneum, a thin layer of fascia, subcutaneous fat and skin. In direct contrast, an omphalocele consists of a defect in the anterior abdominal wall at the umbilicus with little or no attachment or fusion of the normal fascia of the rectus muscles and extrusion of the peritoneal contents into a sac covered only by peritoneum and amniotic membrane.

At the time of delivery, the membrane is transparent, clear and glistening. Within as short a period as three to four hours this glistening surface becomes dull, gray to green in color and thickened, even though it is kept moist with any type of moist compress. After this time the membrane becomes permeable to bacteria, and fatal peritonitis will necessarily follow unless proper surgical intervention is carried out. Because of this relatively rapid change in the membranous covering of the sac, surgical intervention and repair of one type or another of the omphalocele is necessary within a relatively few hours after delivery. The need for operation within a short time has been brought out by Gross [3] in a recent paper; and here again another plea is made for operation as soon as possible after delivery. It is also desirable to operate on these infants within this short space of time before they have swallowed air or formula, which will, necessarily, distend the intestines which are in the sac and, from a mechanical standpoint, will render repair much more difficult.

The series of events leading up to the formation of an omphalocele begins during the first five to ten weeks of fetal life.[4] At this time, the intestinal tract has grown more rapidly than the future peritoneal cavity, and, since the celomic cavity, or future peritoneal cavity, cannot accommodate the rapidly growing intestinal tract, an embryonic, anatomic—or, more simply, a necessary—umbilical herniation results and the gastrointestinal tract extrudes into the base of the umbilical cord. Under normal developmental conditions, at about the end of the tenth week, the future peritoneal cavity has enlarged enough to accommodate the intestinal tract; it is withdrawn, and the defect in the anterior wall of the abdomen closes. If there is abnormal development of the intestinal tract and lack of growth and provision for space in the future peritoneal cavity or if some other peritoneal growth mechanism stops or is delayed, then an omphalocele may result. From that time until the time of delivery any portion of the intestinal tract, liver or spleen or any mobile intraperitoneal structure may remain in the sac. As a portion of the viscera remains in the sac, there will be no further attempt toward formation of an adequate peritoneal cavity.

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3. Gross, R. E.: A New Method for Surgical Treatment of Large Omphaloceles, Surgery **24**:277-292 (Aug.) 1948.

4. Arey, L. B.: Developmental Anatomy: A Textbook and Laboratory Manual of Embryology, ed. 4, Philadelphia, W. B. Saunders Company, 1940.

Omphaloceles vary greatly in size and in contained viscera. The larger the sac and the greater the amount of contained viscera, the greater the mortality. It has been brought out that omphaloceles 10 cm. and above in diameter may carry a mortality of 85 per cent; however, with newer surgical technics and frequently repeated pleas for earlier surgical intervention, this mortality may well be notably decreased. There are a number of reports in the literature of successful repair of omphaloceles.

Surgical management of an omphalocele as a surgical emergency may be a relatively easy and simple procedure, or it may tax the ingenuity of the surgeon when he is confronted with a tremendous sac containing a large portion of the viscera and a distressingly small peritoneal cavity. In small omphaloceles, in which the diameter of the defect in the anterior abdominal wall is below 4 to 5 cm. and the amount of contained viscera is relatively small, the actual mechanical management of the problem is simple. In omphaloceles of this size it is frequently possible to replace the extruded viscera, excise the covering and close the defect. In cases with these smaller sacs the surgeon will be able to do a layer closure, the resulting closure will be strong and the infant will need no further surgical treatment.

In case of a larger omphalocele with an unruptured membrane, more technical difficulties present themselves, both from a mechanical standpoint and from the standpoint of possibly altering the infant's physiologic processes. When the amount of extruded viscera is greater than the peritoneal cavity, then replacement of this extruded material into the small peritoneal cavity by main force and attempted closure of the defect with the replaced material under a moderate amount of pressure will produce the following alterations in the infant: First, there will be elevation of both sides of the diaphragm, with a decrease in the vital capacity of the youngster; hence a series of pulmonary complications could result, or the infant may even become cyanotic owing to the marked decrease in tidal air and vital capacity. Second, placing the extruded material back into the peritoneal cavity under pressure may produce enough pressure on the inferior vena cava and the mesenteric and portal systems to cause circulatory failure because of this increase in intraperitoneal pressure and compression of these venous systems. Third, replacement of the intestinal tract under pressure may lead to temporary intestinal obstruction.

Ladd and Gross first suggested a two stage operation in order to obviate the possible complications due to overcrowding of the peritoneal cavity at the first operation. Their first suggestion was excision of the sac and covering the extruded material with nothing more than

skin flaps, hoping that in time the peritoneal cavity would enlarge enough and the muscles and fascia would stretch enough so that a satisfactory layer closure could be done. This approach was unsatisfactory because the serosal surface of the intestine was being covered by raw subcutaneous fat, which naturally led to multiple adhesions between the loops of intestine and the under surface of the skin flaps; consequently, at the time of secondary operation the dissection of the loops of intestine from the under surface of the skin flaps turned the second procedure into an operation of greater magnitude. Recently, Gross has suggested management of this situation by a method which seems to be much more logical. In his recent cases he has left the membranous sac undisturbed and has merely dissected up lateral skin flaps and brought them over the intact membrane after excision of the cord and then closed the skin flaps over the membranous sac. Theoretically, this would prevent adhesions between the loops of intestine and the skin flaps and make the secondary procedure much simpler, after the muscles and fascia had stretched enough to accommodate the extruded viscera.

In cases in which the membranous covering has ruptured either before or at the time of delivery, the surgeon is confronted with a different problem. There is no membranous covering to protect the intestines from adhesions; hence the surgeon either will have to replace all the eviscerated material and do a layer closure, or if this is impossible will be forced to resort to Ladd and Gross's original suggestion and merely cover the intestines with the raw flaps. In the latter procedure, he will again be faced with multiple adhesions between the skin flaps and the intestinal wall at the time of secondary operation. At the present time no suitable covering has been developed for use as a barrier between the loops of intestines and the raw surfaces of the flaps. Apparently, the use of any of the present oxidized cellulose or gelatin preparations would not be the answer, since it has been demonstrated that as the absorbable material disappears it is replaced with fibroblastic material with the result that after absorption of the material adhesions will still form between the intestine and raw surfaces of the skin flaps.

Recently I have seen a number of omphaloceles that have required several different technics in surgical repair. In the following case reports I am reporting only those cases which demonstrate different technics.

REPORT OF CASES

It has been generally agreed previously that intrauterine rupture of an omphalocele or rupture at the time of delivery carried practically a 100 per cent mortality. I feel that this has been true in the past because too long an interval has been allowed to elapse before surgical

repair was attempted; also, it has been probably true that in cases in which rupture had occurred the intestinal tract and other extruded viscera have been replaced under tremendous pressure and death of the infant was secondary to one or a combination of the three factors mentioned.

Following is a report of successful repair of an intrauterine rupture of an omphalocele.

CASE 1.—Baby boy H., was delivered at 4:15 a. m. on Sept. 12, 1948. The mother, a primipara and primigravida, was at term and had been in labor approximately thirty hours at the time of delivery. Examination within fifteen minutes

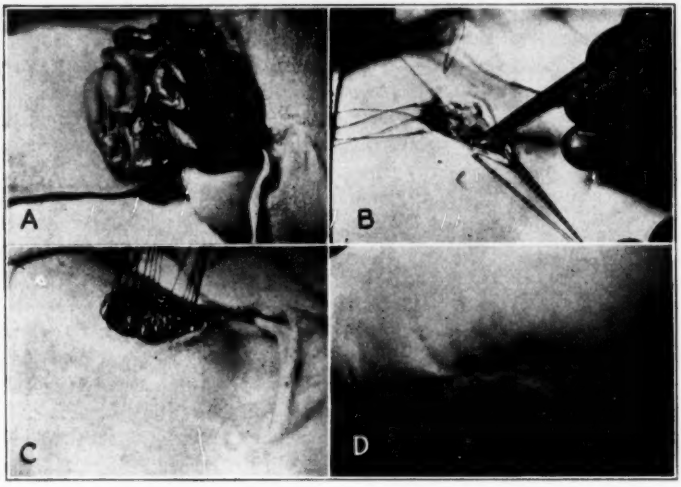

Fig. 1 (case 1).—*A*, amount of extruded viscera. *B*, closure of the peritoneum after replacement of the intestinal tract. *C*, appearance after the edges of the sheath of the anterior rectus muscle have been freshened up and 0000 silk sutures have been placed. *D*, strong anterior abdominal wall at the end of five months. (Reproductions from kodachrome® movie film.)

after delivery revealed that the infant was normal except for the presence of almost the entire intestinal tract herniated through a defect measuring approximately 6.5 cm. in diameter (fig. 1*A*). Apparently, the omphalocele had ruptured early in labor because the individual loops of small bowel were covered with fairly well organized fibrin. Remnants of the membranous covering of the omphalocele were still attached to the margins of the defect, and the umbilical cord was attached to the left side of the opening. Surgical repair was begun within an hour after delivery. The intestines were gently but thoroughly cleaned with warm isotonic sodium chloride solution and further cleansed by application of aqueous merthiolate.® The intestinal tract was replaced with moderate difficulty, but after replacement the peritoneal cavity seemed to be adequate in size and it was felt that undue pressure on the diaphragm, vena cava and portal systems would not be produced.

The edges of the defect were trimmed away, and the peritoneum was closed with continuous suture of 000000 surgical gut (fig. 1 *B*). Edges of the anterior rectus sheaths were then dissected up and closed with 0000 silk (fig. 1 *C*) and the skin defect closed with interrupted silk sutures.

For the first forty-eight hours no milk or formula was given the infant, in order to decrease the amount of distention of the intestinal tract. During this period he was given adequate amounts of fluids subcutaneously and intravenously. After this initial bit of starvation, the infant was started on very small feedings, supplemented with fluids by the subcutaneous and intravenous routes. This regimen was followed for four days, after which time the infant was placed on regular feedings. His postoperative course was entirely satisfactory, and he was discharged from the hospital on the fourteenth postoperative day. His development since that time has been entirely normal, and when last seen, five months after repair, he presented a strong anterior abdominal wall (fig. 1 *D*).

This next case report concerns an infant born with a tremendous omphalocele and a peritoneal cavity much too small to accommodate the extruded material. Unfortunately, I was not called until about six

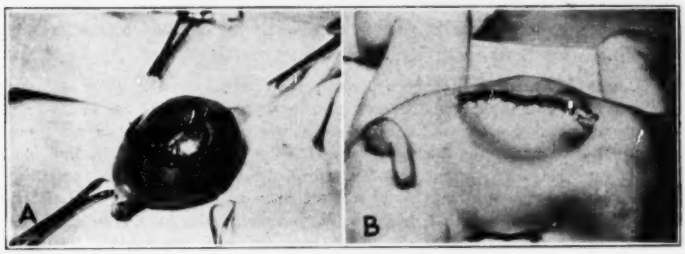

Fig. 2 (case 2).—*A*, preoperative photograph showing the thickened, discolored membranous covering. *B*, appearance of the patient at the end of the operation, done according to the technic recommended by Gross.

hours post partum. Even though the sac had been kept moist with saline compresses during that time, it was very thick, gray-green and obviously permeable to bacteria.

CASE 2.—Baby boy M. was a full term infant. Delivery was difficult because of the omphalocele present. Examination six hours after delivery revealed a 7 pound 6 ounce (3,345 Gm.) child that was normal except for the omphalocele (fig. 2 *A*). The membranous covering of the omphalocele was thickened and discolored. It measured approximately 13 cm. at its base and obviously contained a large portion of the gastrointestinal tract as well as a large portion of the right and left lobes of the liver. An operation was carried out approximately seven hours after delivery. The membranous covering of the omphalocele was thoroughly cleansed with very dilute soap and water and then cleansed with aqueous merthiolate® solution. It was obvious that the peritoneal cavity was too small to accommodate all the viscera contained in the sac; therefore, following the technic advocated by Gross, the membranous covering was not disturbed. Dissection was begun at the junction of the skin and membranous covering and wide undermining of the skin produced skin flaps large enough to allow bringing the skin edges

together over the mass and approximating them without tension (fig. 2 *B*). The immediate postoperative condition of the infant was satisfactory; however, within twenty-four hours after delivery, the infant began to run a septic course and died within fifty hours following operation. The contained viscera were not under undue pressure, since the infant was able to take his feedings regularly and was having normal meconial stools up until twelve hours prior to death.

This infant obviously died from acute fulminating peritonitis, and his case demonstrates how permeable the membranous covering of the omphalocele will become to bacteria within a relatively few hours after delivery.

One of the biggest problems that will confront the surgeon will be the newborn with a ruptured omphalocele in which the defect is large and the amount of extruded viscera is too great to replace without running the danger of one or more of the three complications previously mentioned. In such a case the only type of repair that can be done is dissection of skin flaps large enough to cover the intestine and other extruded viscera, with no attempt directed toward repair of the defect itself. This, necessarily, will lead to troublesome adhesions and a more difficult secondary repair.

Case 3.—Baby boy S. was born prematurely at approximately seven and one-half months with a tremendous defect measuring approximately 7 cm. in diameter. The membranous covering of the omphalocele was ruptured, and it is more than likely that it had ruptured during labor and before delivery, since the individual loops of intestine were covered with fairly firm fibrin. It was obvious at the time of operation that the peritoneal cavity was too small to accommodate these viscera. Since the membranous covering had been destroyed, the only method of repair left was to attempt a skin covering. Accordingly, lateral skin flaps were dissected up and the viscera covered with these raw skin flaps, with the skin closure under no tension. This infant's immediate postoperative condition was fairly good, and for approximately four days he seemed to be on the road to recovery; however, from this time until the time death, six days later, his course was gradually downhill. Apparently, prematurity was the biggest factor in this infant's death, since during the entire postoperative period he had been able to take most of his feedings and was having fairly normal small stools.

SUMMARY

1. The embryologic and anatomic features involved in an omphalocele are discussed.

2. A plea is made for early surgical repair.

3. The types of repair which may be necessary are described and illustrated by case reports.

4. Successful repair of an intrauterine rupture of an omphalocele is described.

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NEW SURGICAL PROCEDURES IN CERTAIN CASES OF CONGENITAL PULMONARY STENOSIS

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AND
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THE TECHNIC of subclavian-pulmonary or aortic-pulmonary anastomosis for the classic case of congenital pulmonary stenosis has been fairly well standardized. Unpredictable findings at operation necessitate use of improved variations in surgical procedures. The following 2 cases illustrate emergency deviations in surgical technic necessitated by anomalies of the pulmonary artery.

CASE 1.—T. K., a girl aged 7 years, weighing 43 pounds (19.5 Kg.), was admitted to the Children's Memorial Hospital, Oct. 12, 1948. She had been mildly cyanotic since birth, became dyspneic on slight exertion and after walking about one block would squat in characteristic fashion.

Physical examination revealed a frail child with cyanosis visible only in the lips, fingers and toes. Suffusion of the conjunctiva was moderate; clubbing of the fingers and toes was minimal. A loud, harsh systolic murmur was heard at the left third interspace along the edge of the sternum. An accompanying thrill was palpable.

Fluoroscopic and roentgenologic examination of the chest revealed a typical boot-shaped heart, avascular pulmonary fields, a rather indefinite pulmonary window and a right-sided aortic arch. The electrocardiogram showed deviation of the axis to the right. The red blood cell count was 6,020,000; the hemoglobin content was 16.4 Gm.

A diagnosis of tetralogy of Fallot with deviation of the aorta to the right was made by Dr. Stanley Gibson. The patient was classed as a good operative risk. Because of the right arch it was decided to perform a subclavian-pulmonary anastomosis on the left side.

Operation (by W. J. P., Oct. 14, 1948.)—Under cyclopropane-oxygen anesthesia administered by Dr. William O. McQuiston, the chest was opened through a posterolateral incision in the left fourth interspace. Sufficient exposure was obtained by separating the ribs with a rib spreader.

The left pulmonary artery was dissected from its bed; it was huge, measuring 1.5 cm. in diameter. A very brisk systolic thrill was palpable at the base of the heart at the point of emergence of the main pulmonary artery.

From the Children's Memorial Hospital and Grant Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

The subclavian artery was isolated and the encircling recurrent laryngeal nerve identified and freed from the adventitia. The subclavian artery was ligated at its point of branching and a ductus clamp[1] applied about 1.5 cm. proximal to the ligature. The artery was then cut just proximal to the point of ligation and drawn out of the loop of the recurrent laryngeal nerve. It measured 6 mm. in diameter.

Constricting ligatures were put around the branches of the left pulmonary artery in preparation for the anastomosis. Very promptly the child showed signs of severe anoxia. The heart slowed and became irregular and the blood pressure dropped alarmingly. The ligatures were promptly released. The aortic clamp was then applied to the pulmonary artery, and a small segment of the vessel

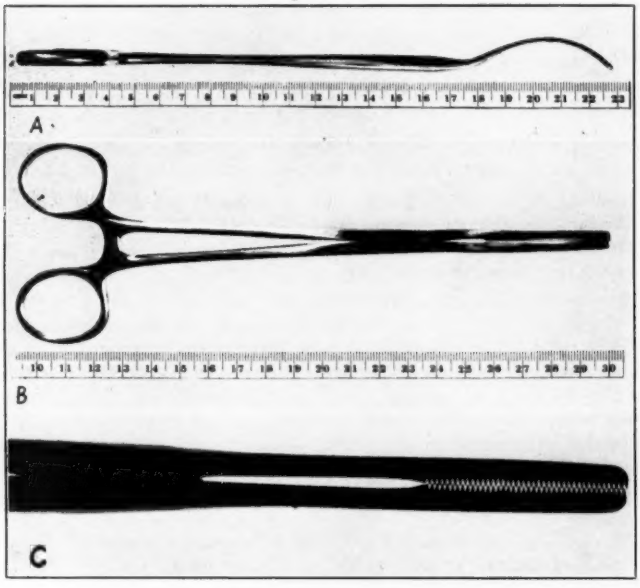

Fig. 1.—*A* and *B*, two views of the curved clamp showing the multiple fine teeth in the apposing jaws. These teeth embed themselves in the adventitia and will occlude but will not injure the vessel. *C*, an enlargement of the ductus clamp to illustrate the arrangement of teeth. There are 40 fine teeth to the inch (2.54 cm.).

was clamped off. Fortunately, before a cut was made in the pulmonary artery, traction was made on the clamp to bring the vessel toward the end of the subclavian artery. As soon as slight traction was made, all signs of severe anoxia promptly returned. A second attempt with similar results made it obvious that very little encroachment on the blood flow in the left pulmonary artery was permissible.

1. Potts, W. J.: A New Clamp for Surgical Division of the Patent Ductus Arteriosus, Northwestern Univ. Med. School Quart. Bull. **22**:321 (Nov.) 1948.

A curved instrument (fig. 1) embodying the same principle as the ductus clamp previously described[1] had been made for a different purpose. The jaws of the clamp are fashioned with many fine teeth which grasp the vessel and occlude it, will not slip and will not injure the vessel. This curved clamp was applied to the left pulmonary artery longitudinally, pinching off a small lateral segment of the vessel (fig. 2). A 6 mm. incision was made in this occluded portion of the pulmonary artery, and an end to side anastomosis was made between it and the proximal end of the subclavian artery. Because the isolated segment of pulmonary artery was small, it was impossible to make the anastomosis intima to intima. The end of the subclavian artery was sutured to the pulmonary artery

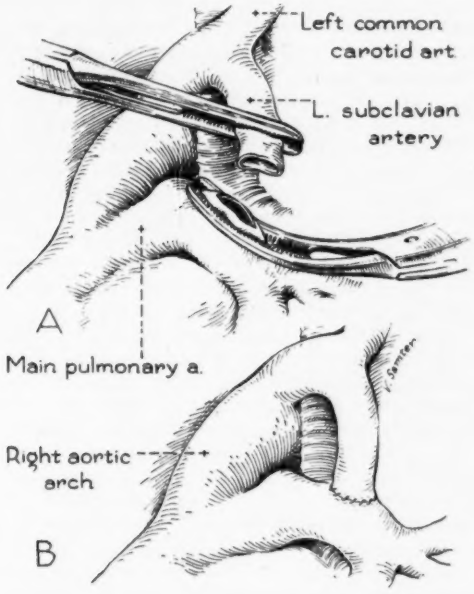

Fig. 2.—*A*, the curved clamp tangentially applied to the pulmonary artery allowing a good portion of the blood to continue to flow through the vessel while the anastomosis is being made. *B*, anastomosis between the subclavian and the pulmonary artery completed with a continuous over and over stitch.

with a single row of continuous over and over stitches of 00000 Deknatel silk. On release of the clamps, there was no bleeding and a brisk continuous thrill was palpable over the anastomotic site. Except for those episodes of anoxia which occurred when the pulmonary blood flow was interfered with, the child withstood the operation well.

The chest was drained with a de Pezzer catheter introduced through the sixth interspace and later connected with a water seal bottle. The lung was reexpanded and the wound closed.

The postoperative course was uneventful. The child was routinely kept in oxygen for twenty-four hours and given 100,000 units of penicillin twice daily for one week. A continuous murmur characteristic of such blood vessel anastomoses could be heard clearly over the left side of the chest anteriorly and posteriorly. All visible cyanosis was relieved. The patient was discharged on the fourteenth day after operation in excellent condition.

On Feb. 4, 1949 the mother reported by telegraph that "Treva walks five blocks to school and back each day. Plays with the other children without restriction. Her color is just like everybody else's. Her appetite was poor but has improved now, and she is doing fine generally."

CASE 2.—L. G. Jr., aged 19 years, entered Grant Hospital Oct. 3, 1948, complaining of slowly increasing cyanosis since infancy and greatly reduced tolerance for exercise. His physical and mental development had been normal.

Physical examination revealed a young man deeply cyanotic with marked clubbing of the fingers and toes and suffusion of the eyes. His weight was 155 pounds (70.3 Kg). His blood pressure was 110 systolic and 85 diastolic. A loud systolic murmur was heard at the second interspace to the left of the sternum. Fluoroscopic and roentgenologic examination of the chest revealed a somewhat enlarged heart which was not typically boot shaped, avascular pulmonary fields, pulmonary window and a right aortic arch confirmed by barium swallow. The electrocardiogram showed deviation of the axis to the right. The red blood cell count was 6,060,000 and the hemoglobin was 18 Gm. A diagnosis of tetralogy of Fallot with a right aortic arch was made by Dr. Frank Dammann.

Operation (by S. S., Oct. 5, 1948).—With the patient under cyclopropane-ether-curare anesthesia, a posterolateral curved subscapular incision was made on the right side. The chest was entered through the base of the fourth rib resected subperiosteally. Cyanosis increased perceptibly when the chest was opened. A large pulmonary artery was identified and dissected from its bed. Complete occlusion of the right pulmonary artery caused immediate cardiac embarrassment. Three times the pulmonary artery was occluded, and each time the heart practically stopped. It was obvious that occlusion of the entire right pulmonary artery for the time necessary to perform an aortic-pulmonary anastomosis or a subclavian-pulmonary anastomosis would not be tolerated.

Dr. McQuiston suggested that the proximal end of one of the branches of the pulmonary artery to the upper lobe might be anastomosed to the side of the aorta. Such a procedure would allow blood to flow through most of the pulmonary artery to the lower and middle lobes while the anastomosis was being made. The large divisions of the pulmonary artery in the hilus of the lung were dissected out, and a branch 5 mm. in diameter, to a segment of the upper lobe of the lung, was chosen. The vessel was occluded proximally with a ductus clamp,[1] ligated distally and cut between. The aortic clamp was applied to the aorta, and in the occluded segment a 5 mm. incision was made (fig. 3). The proximal end of the branch of the pulmonary artery was then anastomosed to the side of the aorta. A silk suture was placed at each end and the anastomosis completed with a single row of continuous 00000 Deknatel braided silk on a curved no. 9 needle. Technically, it was rather difficult to suture the thin-walled pulmonary artery to the thick-walled aorta, but on release of the clamps there was little bleeding and a brisk thrill was palpable over the anastomotic site as blood flowed from the aorta into the pulmonary system. The patient's condition improved immediately.

The lungs were reexpanded. A de Pezzer catheter drain was placed in the sixth interspace and the chest closed in layers with a running suture of surgical gut. The drain was later connected with a water seal bottle.

The postoperative course was uneventful. The drain was removed on the third day. On the patient's discharge from the hospital twelve days after operation, cyanosis was relieved. The red blood cell count had fallen to 5,120,000 and the hemoglobin to 14.6 Gm.

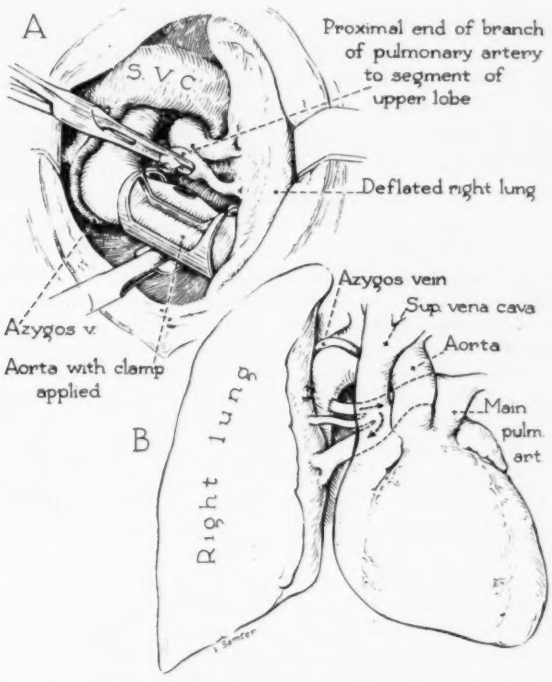

Fig. 3.—*A*, the proximal end of a branch of the pulmonary artery is being held with a ductus clamp. The distal end of this branch has been ligated. A segment of the aorta has been isolated, and a 5 mm. long incision has been made in it. *B*, the anastomosis between the proximal end of a pulmonary artery and the aorta has been completed with an over and over continuous silk suture.

The patient when last seen, Jan. 29, 1949, was in excellent health. No cyanosis was visible, and the tolerance for exercise was tremendously improved. The loud, continuous murmur heard immediately after operation over the right side of the chest has persisted, indicating that the anastomotic channel has remained patent. Little enlargement of the heart has occurred thus far. Clinical and roentgen examinations indicate that no difficulties have arisen from ligating a branch of the pulmonary artery to a segment of the upper lobe.

COMMENT

The fundamental problem in the 2 cases was the same—occlusion of a pulmonary artery for the length of time necessary to perform an anastomosis could not be tolerated. In each case, some blood had to flow continuously through the pulmonary artery to which the systemic vessel was being anastomosed. It must be assumed that in case 1 the left pulmonary and in case 2 the right pulmonary artery were too small to carry enough blood to the lungs to sustain life.

By means of a narrow curved clamp with many fine teeth in the apposing jaws, a crescent-shaped segment of a pulmonary artery may be isolated for anastomosis to a systemic vessel.

It appears from case 2 that the proximal end of a branch of the pulmonary artery may be satisfactorily used for diversion of blood from the systemic to the pulmonic circulation.

DISCUSSION OF PRECEDING PAPERS

Dr. Leon S. McGoogan, Omaha: I should like to comment on the paper by Dr. McLachlin, of Canada, on "Duodenal Obstruction in the Newborn." It has been my unfortunate experience to find that most of the children that I have personally delivered have had multiple lesions of the small bowel and have not been amenable to surgical treatment, and I should like to emphasize again that when one congenital anomaly is found in a newborn infant that a very careful survey be made of the whole child to find other congenital anomalies which may, of course, bar surgical intervention or even any attempt at operation.

As an obstetrician I should like to ask Dr. Maguire what dressing should be placed on an omphalocele sac until the surgeon can get there. Should it be a simple wet saline dressing? Should there be added to the dressing any material such as penicillin until the surgeon can repair the defect?

Is an omphalocele an absolute emergency? Should the surgeon be called within a period of fifteen or thirty minutes after delivery? In case there is a ruptured sac or such a thin sac that there can be no imposition of peritoneum with the closure of the abdomen, is it possible to use transplant of fetal membrane from the placenta? Could the fetal membranes be separated from the placenta and preserved in some sort of solution and used as a graft to help fill in the defect where the peritoneum cannot be used?

Dr. Clifford D. Benson, Detroit: I have observed, as Dr. McLachlin has stated, that obstructions of the duodenum are certainly commoner than was formerly believed. They occur about once in 20,000 cases, and during the past eighteen months I have had 4 cases in addition to those which I reported before this Association two years ago.

I should like to say a few words concerning Dr. Maguire's paper on omphalocele. As he has mentioned, there is a tendency to combine hernia into the umbilical cord and omphaloceles into one group. That may be all right, but I believe that

there is a great difference between hernia into the umbilical cord and omphalocele embryologically. Hernia into the umbilical cord occurs in the eighth to tenth week of embryonic life, whereas omphalocele occurs in the third week. In hernia of the umbilical cord, the problem is one of simply excising the sac and closing the defect, which is a small defect, usually less than 4 cm. in length, where as in the true omphalocele there is a defect of the anterior abdominal wall. In the latter case there is a large defect to be closed, and it presents an entirely different problem. There is a possibility of infection, and also if the sac is not open one will overlook other anomalies which occur in about a third of these patients. In other words, there may be an atresia or stenosis of the intestine. Some of these large defects, 9 or 10 cm. in diameter, cannot be closed in layers; hence we have elected to close them simply by skin closure.

When should one do the second stage closures? That should be determined when one can reduce the contents of the herniation into the abdomen without any discomfort or embarrassment as far as respiratory system is concerned. That must be postponed from six months to twelve months or longer in the large defects.

DR. EDWIN M. MILLER, Chicago: This interesting symposium on children's surgery well exemplifies the rapidly increasing and widespread interest that has been developing in this field since the first successful report of operation for congenital duodenal atresia, by Ernst of Copenhagen in 1916.

There are two points in regard to the paper presented by Dr. Maguire which are worthy of a little more emphasis. First, with due respect to the opinion of D. Penberthy and Dr. Benson, I believe very strongly that it is a good idea wherever possible to maintain intact this delicate cellophane-like transparent covering for the viscera in the infant born with the large omphalocele. Too often this has already been ruptured when we first see these little patients, or too often, therefore, peritonitis is already present. The need for immediate operation is quite apparent, and the objective is to secure a covering of skin, as Dr. Maguire has so well shown in his colored movie. These wounds, because of tension, do not always heal by primary union, and some of the stitches gradually give way leaving areas of granulation tissue which become covered slowly by a rough, thick, epithelial surface.

Second, there is no hurry, as I see it, about performing the second operation. In fact, it is wise to allow several months, or better still, several years to pass by, and during this waiting period good use is made of a wide elastic supporting band. One of my little patients, upon whom I operated in 1933, now is a full grown young woman and well illustrates the good result which can be obtained by observing the points which we have here endeavored to stress.

DR. R. K. GILCHRIST, Chicago: I emphasize some points of our case of tracheoesophageal fistula because the diagnosis is so easily missed. This man had several drinks, but he was not really drunk when he was brought to the hospital. He was not sick. He was not knocked out. He had coughed up a little blood. I did not see him until two days later. No one thought much about it until the second morning, when Dr. Albi said, "When he drinks he strangles." They had just given him a swallow of iodized oil which filled the lower bronchi. He had no emphysema. The fistula occurred at exactly the same spot where a similar one occurred in a man in the Navy who had a heavy box strike him a glancing blow across the upper part of the chest. That man manifested emphysema, and he had to have a tracheotomy before his fistula was repaired. This tear

occurs where the trachea and the esophagus are in their most intimate contact. I suppose that there is some sort of hyperextension mechanism pulling downward that snaps the trachea and esophagus like a rubber band and tears them. Obviously, chemotherapy helped prevent mediastinitis, but if the diagnosis had been made in the first few hours the treatment would have been different. I am also sure that the feeding by the tube passed beyond this fistula is not a particularly safe one and one is better off to do a gastrostomy and feed the patient immediately.

There is no particular trick to doing the operation as far as separation of the tract goes, since there is good firm scar tissue; there is also no likelihood of stirring up a still dormant infection. The mediastinal pleura should be left open after the tract has been separated so that mediastinitis does not develop if there is a leak.

We think that in this patient—who was not a good patient and who was a prisoner of the police under arrest at the time and who rejected everything that was done—the interposition of the flap of pleura probably prevented the reestablishment of the fistula when he was eating food that was brought to him on the side by his family. He is perfectly well now.

Dr. John K. Ormond, Detroit: As one of the very few urologists who are members of this Association, I should like to congratulate Drs. Lich, Maurer and Burdon on their presentation. I was particularly interested in their application to children. It is very promising. As a background, I might state that I have tried the method they spoke of only 3 times. My colleagues and I still use the one stage suprapubic prostatectomy in about half our cases. In a little less than half we have used the transurethral operation route, saving the perineal route for the radical procedures for carcinoma.

One thing that has given us pause in adopting the retropubic method is the fear of osteitis pubis. I notice in their report that the authors spoke of having seen a certain number of cases of osteitis pubis. I should like to ask them to say how quickly it occurred and how long before the patients recovered.

Dr. Robert M. Wansbrough, Toronto, Canada: I am always stimulated by my old colleague, Dr. McLachlin, because he delves into things that many persons neglect. The duodenal atresias are not rare at all; they are just not diagnosed. This is truer in a large number of lesions in children than it is in adults. There are two or three things that Dr. McLachlin spoke of that I feel are very important. In new babies, the vitality is low and they are suffering from malnutrition. I therefore feel it is most important that the viscera are handled very gently, and, as many of these patients have some degree of failure of rotation, I do not believe it is wise to attempt to return the viscera to a normal anatomic position.

Dr. Henry K. Ransom, Ann Arbor, Mich.: I should like to comment on Dr. Leahy's paper and report a case that I observed last year, a case of congenital pulmonary tension cyst in a little child 3½ months old. The child was brought in cyanosed, presenting a typical picture. A roentgenogram showed the mediastinum pushed far over to the opposite side and a needle was inserted into the cyst for the immediate relief. The child at the time it came in had a little fever (temperature up to 100.1 F.). There were rales on his good side and marked atelectasis in both upper and lower lobes of both lungs so one could hardly see the lobes and would not be sure they were present on the first roentgenogram. With repeated films one could tell that the upper and lower lobes were present and that the cyst probably arose from the middle lobe. We kept

the child under aspiration until his temperature came down to normal, approximately five or six days, and took out the cyst. The cyst was unbelievably simple to remove. The minute I made an anterior incision across the front of the chest —and the needle was out of the cyst at that time—the cyst ballooned right out, and it was practically unnecessary to use a retractor. The child's face was a little blue on the second day. The needle stopped draining, and I suggested that a tube be put in. I took the child to the dressing room, made a little niche, put in a trocar and slipped the tube in 3 or 4 cm. and the air came back into the bottle. Next morning the attendants said that air had stopped coming through the tube. The child was just starting to get blue again. We checked immediately with the roentgenogram, and the tube was lying between two layers of pleura outside the cyst, and the air had been leaking through and in that had become blocked off.

Dr. Anthony R. Curreri, Madison, Wis.: From the several papers presented this morning, it must be obvious that, at least in so far as operation in young infants is concerned, procrastination is not indicated. I should like to say a little more about Dr. Leahy's paper. Undoubtedly, with the combined efforts of surgeons, pediatricians and anesthetists many infants can have the advantage of exploration with minimal injury and with an opportunity to obtain excellent results. Thoracic lesions mimic one another. For example, emphysema may mimic tension pneumothorax. A mediastinal gastric cyst has masqueraded as pneumonia and whooping cough in one of our cases, and other mediastinal cysts have been considered thoracic tumors. Congenital cysts are often treated by physicians by procrastination and conservative therapy until secondary infection occurs. At this time, everyone is excited and immediate operation is requested. Here the problem is one of resection when the cysts are free from infection. At that time operation is simple, and the child's immediate postoperative course excellent. Surgical procedures during a period of acute infection are associated with toxemia, acute inflammatory reaction and nodes about the hilar structures. Thus, dissection of the bronchi and vessels is extremely difficult and the immediate postoperative course is much more violent.

Dr. Robert Lich, Louisville, Ky.: In regard to Dr. Ormond's questions, I should like to say that in our own work the number of transurethral resections is approximately 40 per cent. When we started our series of retropubic prostatectomies eighteen months ago, we did the first 100 prostatectomies by this method more or less to determine the limitations of this operation.

In so far as osteitis pubis is concerned, this condition occurred in 2 patients. The first patient was hugely obese and severely diabetic and was incapacitated almost 100 per cent, I should say, for a matter of about five weeks, and thereafter he was only partially incapacitated. The other was a man who had very little actual incapacitation. He was able to carry on his usual activities, although he complained of considerable pain in the pubic region. I cannot go into the cause and the whole problem of osteitis pubis, but I should like to mention that one of the severest instances of osteitis pubis that I have ever seen followed a perineal prostatectomy in which the patient was hospitalized intermittently for almost six months. I noticed recently that Drs. Rosenberg and Vest reported 2 instances of osteitis pubis following transurethral resection.

In conclusion, one can only say that to date in the American literature osteitis pubis constitutes the greatest hazard to retropubic prostatectomy. Our experience, however, has not been sufficiently alarming to discard the operation.

DR. WINFIELD L. BUTSCH, Buffalo: It seems to me that aspiration of pulmonary cysts carries with it considerable danger: first, that the aspiration may be followed by an immediate collapse of the lung and pneumothorax, thus precipitating a respiratory crisis, and, secondly, that the procedure may be followed by infection with toxemia. The delay connected with aspiration may also be accompanied with infection in other portions of the lung, due to the continued pressure of the cyst. Therefore, Dr. Butsch and I agree with the discussers that aspiration should be used either not at all or only for a temporary period to allow adjustment of the infant's physiologic state. We have found 4 instances in the literature of the removal of lungs or lobes in infants under 1 month of age, to add to the 3 that we reported today. Dr. Gross performed a pneumonectomy on the infant at the age of 3 weeks; Dr. Bailey, lobectomy of the right upper and middle lobes at the age of 1 month; Dr. Chisholm, lobectomy at the age of 5 days, and Dr. Burnett, lobectomy at the age of 15 days. All these operations were successful.

DR. A. D. MCLACHLIN, London, Ontario: Dr. Benson has asked about the comparative value of duodenojejunostomy and gastrojejunostomy. The second patient had had a duodenojejunostomy first and then a gastrojejunostomy because the duodenojejunostomy had not functioned within what we thought was an adequate amount of time. At the end of a year, however, roentgenograms showed that only the anastomosis between the duodenum and jejunum was functioning. If the fine catheter had been passed through the duodenojejunostomy, it is unlikely that the second operation would have been necessary.

Dr. Miller spoke of the possibility of other anomalies in these patients. I believe we were rather lucky here in having 4 cases with what seems a single congenital defect. Three of the patients are now more than a year old and are making apparently normal progress.

I agree with Dr. Wansbrough regarding the necessity for gentleness in children's surgery. The last of these patients had almost succumbed to exploration in the depths of the abdomen. Four days later this same baby, still having had no food by mouth, underwent a duodenojejunostomy in which there was no other handling with minimal disturbance. It seems that children are superior to adults in surviving operative procedures in everything except their ability to stand rough handling. If the operative procedure can be completed with a minimal amount of trauma, their chance of survival seems greater than in the adult.

DR. C. H. MAGUIRE, Louisville, Ky.: In regard to Dr. McGoogan's question as to what dressing should be placed on the omphalocele, I do not consider that of too much importance. In the second case, in which the membranous covering was quite thick and dirty gray, that youngster had been kept with a saline compress from the time of delivery until it was decided what to do. One wonders whether the use of any antibiotic as a compress might not irritate the membranous covering which, after all, is nothing more than peritoneum.

To the question as to whether or not an omphalocele is an absolute emergency I think the answer is yes. The longer one delays, the less the chance of recovery. Several surgeons have tried letting the big omphaloceles go for a period of weeks, and practically all the cases have ended fatally.

The skin makes an effort to climb over this membranous covering, but in practically all cases of that sort ulceration of the membranous covering occurred and the patients died of the ensuing peritonitis. I was interested in the possibility of the use of the fetal membrane. I certainly think that is one thing that might be considered. As far as I know, nobody has tried it.

I agree with Dr. Benson that a simple herniation into the umbilical cord is not an omphalocele and does not require an extensive surgery.

I agree with Dr. Miller, and take issue with Dr. Benson, in that I do not believe that we should sacrifice the membranous covering, even with the possibility of carrying in a little infection. The use of the membranous covering certainly makes the secondary operation much simpler.

Interestingly, in the infant who died of fulminating peritonitis the space between an apparently dirty membranous covering of the omphalocele and the subcutaneous fat was entirely clean. The infection had already gone through the membranous covering prior to operation. It was not the introduction of the membranous covering into the wound that brought peritonitis.

A METHOD FOR CONTROL OF BLEEDING FROM ESOPHAGEAL VARICES

THOMAS B. PATTON, M.D.
AND
CHARLES G. JOHNSTON, M.D.
DETROIT

ONE OF the most dramatic and hazardous types of bleeding from the gastrointestinal tract is that from esophageal varices. Esophageal varices commonly occur in association with cirrhosis of the liver. In such instances the dilated esophageal vessel is a reflection of increased tension in the portal system. Several methods have been devised for controlling hemorrhage from varices, most of them being a direct attack on the varix itself. In 1939 Crafoord and Frenckner[1] described the nonsurgical treatment of varicose veins by injection of a sclerosing solution under direct vision. Phemister[2] in 1947 reported 1 case with treatment by total gastrectomy and 1 with treatment by esophagogastric resection for bleeding esophageal varices in Banti's syndrome. None of these methods attempt to control the cause of the varix but, rather, attempt to treat the varix itself by removal of the dilated veins or by an attempt to cause clotting within the veins. More recently the work of Blakemore[3] has suggested a method for lowering the portal pressure by means of portacaval or splenorenal vein anastomoses. It has been our experience that bleeding from esophageal varices has provided us with the most clearcut indication for anastomoses between the portal and the caval systems. For such procedure it is best that the patient be in as good condition as is possible. Our interest was turned to a

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1. Crafoord, C., and Frenckner, P.: Non-Surgical Treatment of Varicose Veins of the Esophagus, Acta Oto-Laryng. **27**:422, 1939.

2. Phemister, D. B., and Humphreys, E. M.: Gastro-Esophageal Resection and Total Gastrectomy in the Treatment of Bleeding Varicose Veins in Banti's Syndrome, Tr. Am. S. A. **65**:17 (Oct.) 1947.

3. Blakemore, A. H.: Portacaval Anastomosis, Surgery **24**:480 (Sept.) 1948.

controllable method of hemostasis in order that patients might be preserved for study and be prepared for portal decompression.

This problem has received attention from several investigators. Westphal,[4] in 1930, used tamponade for bleeding esophageal varices by means of the Gottstein sound. He reported 2 cases in which control

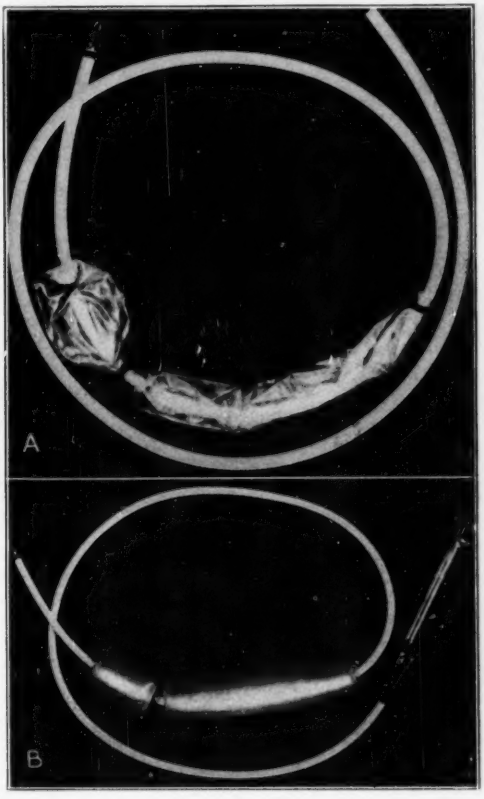

Fig. 1.—Double balloon tube, *A*, and, *B*, inflated.

of the bleeding was secured. As far as we can determine, this method received little attention, being mentioned by Kaplan [5] in 1941. In 1947,

4. Westphal, K.: Compression Treatment in Hemorrhage from Esophageal Varix, Deutsche med. Wchnschr. **56**:1135 (July 4) 1930.

5. Kaplan, B.: Esophageal Varices, M. Rec. **154**:176 (Sept. 3) 1941.

Rowntree [6] and his associates described an inflatable balloon used to control bleeding from esophageal varices in two cases. Tocantins,[7] in 1948, mentions the use of the balloon tampon for control of esophageal hemorrhage, and Bixby,[8] in the same year, described the use of the Miller-Abbott tube for control of hemorrhage from the same area.

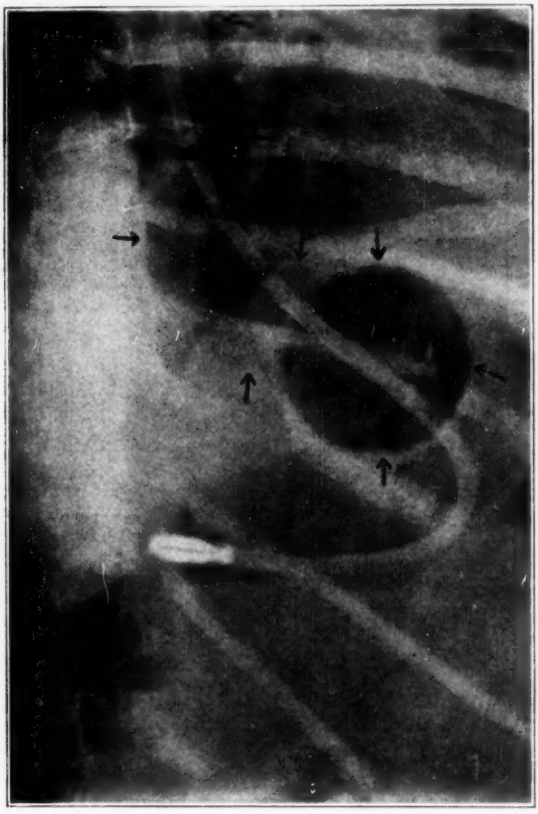

Fig. 2.—Roentgenogram showing double balloon tube in place.

6. Rowntree, L. G.; Zimmerman, E. F.; Todd, M. H., and Ajac J.: Intra-esophageal Venous Tamponage, J. A. M. A. **135**:630 (Nov. 8) 1947.

7. Tocantins, L. M.: The Hemorrhagic Tendency in Congestive Splenomegaly (Banti's Syndrome), J. A. M. A. **136**:616 (Feb. 28) 1948.

8. Bixby, E. W., Jr.: Correspondence, J. A. M A. **138**:908 (Nov. 20) 1948.

We have tried the methods recently described by the various authors, but in our hands these proved unsatisfactory, since it was difficult to ascertain and maintain the position of the tube. In several cases the tube passed into the stomach or into the upper reaches of the esophagus.

We have used a plastic tube [9] of the type described by Honor and Smathers,[10] but having four lumens. A Rehfuss tip of sufficiently small size to pass through the nares is incorporated into the end of the largest lumen of about 4 feet (122 cm.) of tubing. Eight inches (20 cm.) above this a balloon of rubber, of the consistency of glove rubber, is tied on. Immediately above this and contiguous with this balloon, an additional balloon made of an entire condom is applied. The two balloons are, of necessity, separately inflatable.

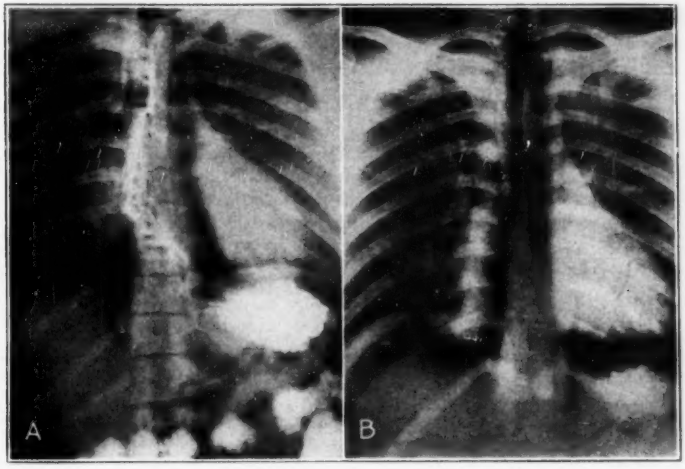

Fig. 3 (case D. S.).—Esophagrams (*A*) prior to and (*B*) one month after portacaval shunt.

The tube is passed through the nares and into the stomach, its position being proved by aspiration. The lower balloon is then inflated to such a degree as to give a diameter of 2½ to 3 inches (6.4 to 7.6 cm.), the tube is pulled up so that the balloon engages snugly at the cardia, which acts as an anchor on the gastric side. The tube is then taped to the nose and the upper balloon is inflated with 200 to 250 cc. of air. The tube is left in place for twelve hours with constant suction

9. Supplied by Payette and Henning, 2238 Second Street, Wyandotte, Mich.

10. Honor, W. H., and Smathers, H. M.: A Double-Lumened Plastic Tube for Intestinal Intubation, Arch Surg. **55**:498 (Oct.) 1947.

within the stomach. The upper balloon is deflated after the twelve hour period, and if there is evidence of bleeding it is again inflated and left in place for an additional twelve hours.

The third small lumen may be used for the administration of thrombin [11] after the method of Daly,[12] the thrombin being introduced just above the upper balloon.

After the arbitrary period of twelve hours has elapsed, it has been our practice to deflate the balloons; if bleeding has stopped, material aspirated from the stomach will be free of blood. The tube, however, is left in place. The patient is started on sips of fluid and is gradually placed on a full diet about the third day. Supportive treatment also must be carried out during the procedure.

We have used the tube successfully in 6 cases and have had 2 failures; 1 was in the case of a moribund patient in which the balloons were not checked to see that they were adequately inflated. In the other case at final examination the patient was found to have a bleeding duodenal ulcer.

Following is an illustrative case.

D. S., a 25 year old white man first vomited blood in May 1946. A diagnosis of Banti's disease was made and splenectomy with ligation of coronary veins performed in August 1946. He was well until October 1948, when he vomited blood. Bleeding was controlled by means of the double balloon tube, and a portacaval shunt was performed in November 1948; follow-up in February 1949 revealed that the patient was well, was working at his former job and had gained 30 pounds (9.1 Kg.).

SUMMARY

1. A quadruple-lumened plastic tube with two inflatable balloons is presented as a means of control of hemorrhage from esophageal varices.

2. A total of 8 patients have been treated, with 2 failures.

ADDENDUM.—Since the presentation of this paper, we have been informed by a personal communication from Dr. A. H. Blakemore that he has used tamponade successfully as a means of control of bleeding esophageal varices prior to the elective shunt procedure.

Dr. William H. Honor assisted in this study and gave technical advice.

11. Warner, E. D.; Brinkhous, K. M.; Seegers, W. H., and Smith, H. P.: Further Experience with the use of Thrombin as a Hemostatic Agent, Proc. Soc. Exper. Biol. & Med. **41**:655 (June) 1939.

12. Daly, B. M.: Use of Buffer Thrombin in the Treatment of Gastric Hemorrhage, Arch. Surg. **55**:208 (Aug.) 1947.

EXPERIENCES WITH ISLET CELL TUMORS

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AND
BROCK E. BRUSH, M.D.
DETROIT

IN 1924, just two years after the discovery of insulin by Banting and Best,[1] Harris[2] published his report on "Hyperinsulinism and Dysinsulinism," having noted in several patients a clinical picture similar to that caused by overdosage of insulin. Nicholls,[3] in 1902, first described the finding at autopsy of an islet cell tumor, but the possible clinical significance was not recognized until this syndrome simulating insulin shock was described by Harris. In 1926 Warren[4] reviewed 20 cases of islet cell hypertrophy observed at autopsy, in only a few of which were there significant symptoms of hyperinsulinism. According to Bockus,[5] an estimated 80 per cent of proved cases of islet cell tumors are clinically silent lesions, giving no symptoms of hyperinsulinism. The first case in which operation was done for an islet tumor was reported by Wilder, Allan, Power and Robertson[6] in 1927. An extensive islet cell carcinoma with metastases was found, and the patient survived only a few weeks. The first successful removal of an islet cell tumor for hyperinsulinism was performed in 1929 by Roscoe Graham, reported by Howland, Campbell, Maltby

From the Department of General Surgery, Henry Ford Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Feb. 18, 1949.

1. Banting, F. G., and Best, C. H.: Internal Secretions of the Pancreas, J. Lab. & Clin. Med. **7**:251, 1922. Banting, F. G.; Best, C. H., and others: Pancreatic Extracts in the Treatment of Diabetes Mellitus, Canad. M. A. J. **12**:141, 1922.

2. Harris, S.: Hyperinsulinism and Dysinsulinism, J. A. M. A. **82**:729 (Sept. 6) 1924.

3. Nicholls, A. G.: Simple Adenoma of the Pancreas Arising from an Island of Langerhans, J. M. Research **8**:385, 1902.

4. Warren, S.: Adenomas of the Islets of Langerhans, Am. J. Path. **2**:335, 1926.

5. Bockus, H. L.: Gastroenterology, Philadelphia, W. B. Saunders Company, 1946.

6. Wilder, R. M.; Allan, F. N.; Power, M. J., and Robertson; H. E.: Carcinoma of the Islands of the Pancreas: Hyperinsulinism and Hyperglycemia, J. A. M. A. **89**:348 (July 30) 1927.

and Robinson,[7] and this patient is alive and well today. Approximately 140 patients with islet cell tumor have been operated on, and in another 50 the tumors have been found at autopsy examinations. Whipple[8] has had by far the largest experience, having personally operated on over 25 of these patients.

CLINICAL FEATURES

The syndrome of hyperinsulinism may be varied in its manifestations, and also the "attacks" or "spells" vary widely in severity in the same patient. Mild manifestations, marked by fatigue and exhaustion, may exist a considerable length of time before severe attacks of convulsion or loss of consciousness occur. The symptoms usually include weakness, sweating, hunger, paresthesias, pallor, dizziness, palpitation, inability to move the extremities and perhaps syncope. Much of this picture may be caused by the release of epinephrine in an attempt to elevate the blood sugar level. Wilder[9] has grouped the symptoms under those related to the central nervous system, those related to the autonomic nervous system and, finally, the psychic disturbances.

DIAGNOSIS

It must be strongly emphasized that spontaneous hypoglycemia is by no means pathognomonic of an islet cell tumor. Since hypoglycemia is a common condition and hyperinsulinism is rather rare, great care must be exercised in the diagnosis of an islet cell tumor. Many organs are involved in the maintenance of a normal blood sugar level. The importance of the liver and the pituitary, adrenal and thyroid glands in addition to the pancreas has become recognized, with the result that investigation of hypoglycemic symptoms includes studies of these various organs. An etiologic classification of spontaneous hypoglycemia proposed by Conn[10] includes the various conditions which must be considered. Insistence on the presence of the "Whipple triad"[8] as an indication for surgical intervention will result in the finding of a tumor in a large percentage of cases. This triad includes nervous system disorders, such as confusion, coma, convulsions or collapse, coming on in the fasting state, accompanied with a blood sugar level of 50 mg.

7. Howland, G.; Campbell, W. R.; Maltby, E. J., and Robinson, W. L.: Dysinsulinism, Convulsions and Coma Due to Islet Cell Tumor of the Pancreas, with Operation and Cure, J. A. M. A. **93**:674 (Aug. 31) 1929.

8. Whipple, A. O.: Hyperinsulinism in Relation to Pancreatic Tumors, Surgery **16**:289, 1944.

9. Wilder, R.: Clinical Diabetes and Hyperinsulinism, Philadelphia, W. B. Saunders Company, 1941.

10. Conn, J. W.: The Spontaneous Hypoglycemias, J. A. M. A. **115**:1169 (Nov. 16) 1940.

or less per hundred cubic centimeters and relief of these symptoms by the administration of glucose. Repeated fasting blood sugar values of 50 mg. or less when the patient is on a normal diet are fairly conclusive. We [11] have felt that glucose tolerance and phosphorus curves are of considerable diagnostic aid if a proper preparatory diet has been used prior to the tests.

PATHOLOGY

A certain number of islet tumors have had malignant characteristics microscopically, yet their clinical course has been that of a benign condition. This fact has led Frantz [12] to classify them as benign, malignant and questionable. In 1940 Frantz reported 8 cases of questionably malignant tumors from Whipple's series and collected 16 others in which there was no return of symptoms after many years. Perhaps some of the cases reported by Allan and Marshall [13] in which the tumors were diagnosed as of low grade malignancy by Warren fall into this category. Only about 15 cases of unquestioned malignant islet cell tumors in which metastases to the lymph nodes or liver have occurred have been reported. Marble and McKittrick [14] reported 1 such case in their group of 6 cases of islet cell tumors.

SURGICAL TREATMENT

Since in about 15 per cent of the reported cases islet cell tumors have been found to be multiple, careful exploration and palpation of every part of the pancreas is of great importance. If a very careful search of the complete organ does not reveal a tumor, a subtotal pancreatectomy should be performed, with removal of at least four fifths of the gland. Removal of a small portion of the gland in such cases has given uniformly poor results, but subtotal resection has given excellent results in cases reported by Graham,[15] David,[16] Womack [17] and us.[11] According to Duff,[18] tumors which produce the hypoglycemic syndrome

11. Brush, B. E., and McClure, R. D.: Hyperinsulinism Treated by Subtotal Pancreatectomy, Ann. Surg. **120**:750, 1944.

12. Frantz, V. K.: Tumors of the Islet Cells with Hyperinsulinism; Benign, Malignant and Questionable, Ann. Surg. **112**:161, 1940.

13. Allan, F. N., and Marshall, S. F.: The Surgical Treatment of Islet Tumors of the Pancreas with Hyperinsulinism, S. Clin. North America **25**:719, 1945.

14. Marble, A., and McKittrick, L. S.: Islet Cell Tumors of the Pancreas with Hyperinsulinism, New England J. Med. **235**:637, 1946.

15. Graham, E. A., and Hartman, A. F.: Subtotal Resection of the Pancreas for Hypoglycemia, Surg., Gynec. & Obst. **59**:474 (Sept.) 1934.

16. David, V.: The Indications and Results of Pancreatectomy for Hypoglycemia, Surgery **8**:212, 1940.

17. Womack, N.: Hypoglycemia, Surgery **2**:793, 1937.

18. Duff, G. L.: Pathology of Islet Cell Tumors of the Pancreas, Am. J. M. Sc. **203**:437, 1942.

are usually always over 1 cm. in diameter, yet in many cases they are difficult to detect, as evidenced by the number of tumors missed at the first operation and found later when symptoms persisted. Priestley, Comfort and Radcliffe [19] reported a successful total pancreatectomy for a very small tumor which could not be seen or palpated but was found on pathologic sectioning of the gland.

When a tumor has been completely removed, the clinical results are always excellent, and when such a result is not obtained one must seriously consider the probability that a second tumor has been overlooked at the time of operation either in the pancreas or possibly in some ectopic pancreatic tissue.

REPORT OF CASES

The essential features of our 5 cases of hyperinsulinism are presented. Three of these cases have been reported previously elsewhere.[20]

CASE 1.—M. B., a white woman, age 19, was first seen April 11, 1935. Her chief complaints were severe headaches and abdominal cramps. Fasting blood sugar levels were 78 and 99 mg. per hundred cubic centimeters.

In January 1936, the patient complained of frequent attacks of weakness, sweating, tremor and a mental reaction described as stuporous. These attacks were relieved by the ingestion of carbohydrate. A glucose tolerance test revealed that the glucose was utilized rapidly, with a fall to 43 mg. per hundred cubic centimeters in ninety minutes. At operation, Feb. 10, 1936, a tumor was not found and a subtotal pancreatectomy was done. The patient is alive and well today and utilizes glucose normally.

CASE 2.—M. C., a white woman aged 43, was first seen in August 1942, with the complaint of attacks of nervousess, weakness, sweating and hunger, occurring about three hours after eating. These attacks were made worse by exercise and relieved by eating. After a trial on a high protein, low carbohydrate diet, the patient was operated on April 22, 1943. No discrete tumor was found, and a subtotal pancreatectomy was performed. The patient has had no return of symptoms and has normal glucose tolerance.

CASE 3.—G. Y., a white woman aged 40, was first seen on Nov. 13, 1946, complaining of attacks of weakness, blurred vision, slurred speech, profuse sweating and, if not aborted by the ingestion of carbohydrate, syncope lasting from one-half hour to two hours. These attacks had begun two years before and had become progressively worse. The patient was 5 feet 8 inches (173 cm.) in height and weighed 230 pounds (104.3 Kg.); the excess weight had been gained largely in the preceding two years.

Results of liver function tests were normal; the basal metabolic rate was —13 per cent, and a series of determinations of fasting blood sugar averaged 47 mg. per hudred cubic centimeters. Oral and intravenous glucose tolerance tests were completed with difficulty because of hypoglycemic reactions. The intra-

19. Priestley, J. T.; Comfort, M. W., and Radcliffe, J.: Total Pancreatectomy for Hyperinsulinism Due to an Islet Cell Adenoma, Ann. Surg. **119**:211, 1944.

20. (*a*) Brush and McClure.[11] (*b*) Kuffel, M. J.; Foster, D. P., and Lowrie, W. L.: Hyperinsulinism with Hypoglycemia Relieved by Removal of Pancreatic Tumor, Am. J. Digest. Dis. **14**:279, 1947.

venous test curve showed a level of 34 mg. per hundred cubic centimeters one and one-half hours after the administration of glucose and 44 mg. at five hours. At operation a nodule 2 cm. in diameter was removed from the head of the pancreas. The patient thereafter lost weight, and her blood sugar level returned to normal with relief of the symptoms.

CASE 4.—J. P., a white woman aged 28, first seen April 15, 1947, complained of spells of "loss of awareness of her surroundings," incoherence, numbness in the extremities, face and lips and perspiration. These frequently came on in the morning before breakfast and were often accompanied with headaches. Relief from ingestion of carbohydrates was dramatic. Blood sugar levels during attacks

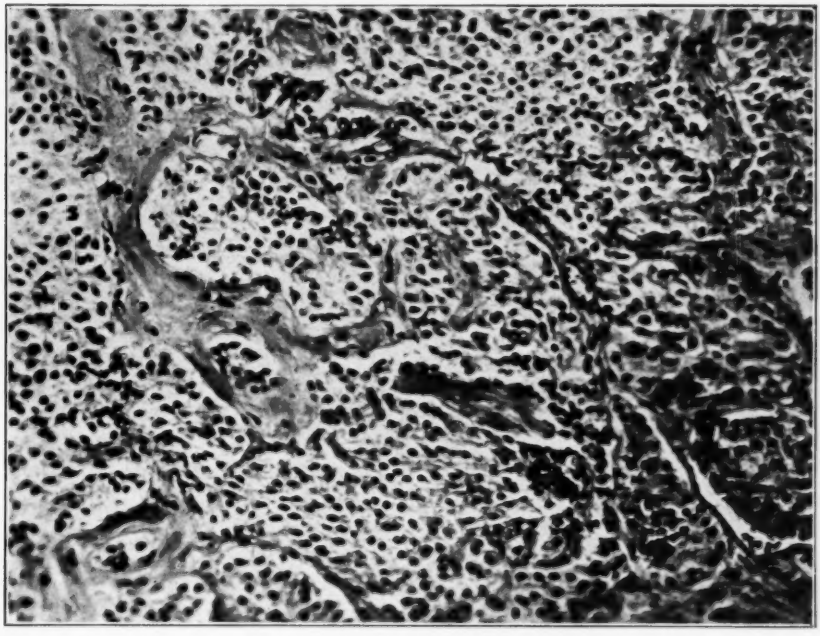

Fig. 1 (case 4).—Islet cell adenoma.

ranged from 32 to 37 mg. per hundred cubic centimeters. The basal metabolic rate was —2 per cent. Results of liver function tests were normal, as was the electroencephalogram; stereoroentgenograms of the skull revealed no abnormalities. At operation, on June 6, 1947, an islet cell adenoma 1.5 cm. in diameter was removed from the head of the pancreas (fig. 1). In May 1948 an epigastric swelling appeared, and a pseudocyst of the pancreas was diagnosed. On June 2, 1948, 400 cc. of material was aspirated and the cyst marsupialized. After six weeks small amounts of sodium morrhuate were instilled, and complete healing occurred three weeks later. The patient has had no return of symptoms from the adenoma or the cyst, and her blood sugar levels are within normal limits.

CASE 5:—H. J., a white man aged 45 years, was first seen in June 1947, complaining of attacks of dizziness, staggering, disorientation, weakness and collapse. These attacks had begun only six months previously and had become progressively worse. Carbohydrate relieved the symptoms. Blood sugar levels during the attacks ranged from 35 to 45 mg. per hundred cubic centimeters, and the tolerance curve was flat. A roentgenogram showed narrowing of the second portion of the duodenum.

At operation, on July 12, 1947, a large encapsulated tumor was noted along the upper border of the pancreas in the region of the neck. The tumor was removed. It weighed 50 Gm. and on microscopic section proved to be an adeno-

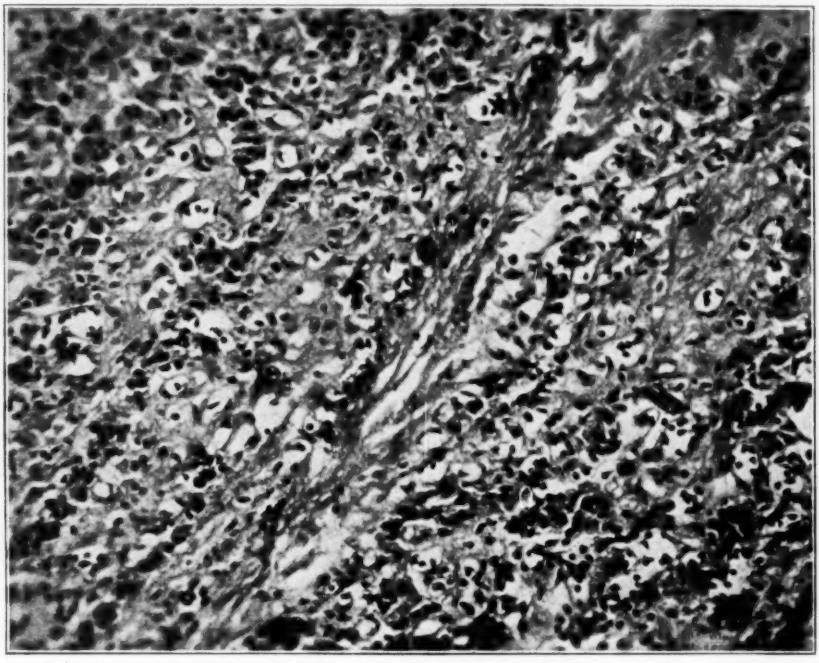

Fig. 2 (case 5).—Islet cell carcinoma.

carcinoma (fig. 2). A large lymph node in the gastrohepatic mesentery was removed, and it was found that the normal tissue had been completely replaced by tumor tissue. Because of the failure to recur in many of cases of tumor of low grade or suspected malignancy and the definite encapsulation of this tumor, it was thought that possibly after wide excision of the tumor and the involved lymph nodes cure might be obtained. However, the symptoms of hyperinsulinism gradually returned, and, in view of the disappointing results of alloxan therapy, a more radical operation was undertaken. A total pancreatectomy was performed on July 14, 1948 with great difficulty because of the extension of the growth. The patient died on the fifth postoperative day.

COMMENT

Our 5 cases represent the three situations that may be found at operation: no discernible tumor, an islet adenoma and an islet cell carcinoma. In the 2 cases in which a tumor was not found and a subtotal resection was performed and in the 2 cases in which a benign adenoma was found and removed, equally good clinical results were obtained. In the case of carcinoma with metastases there was recurrence of the tumor, as there has been in all other reported cases. The development of a pancreatic cyst, which occurred in 1 case, is a fairly common complication encountered in operation on the pancreas and is usually handled very well by marsupialization.

In most instances the pancreas can best be completely examined by an approach through the gastrocolic omentum; however, in 2 of our cases the tumor was removed by incising the gastrohepatic omentum and employing downward traction on the stomach. The importance of frequent determinations of blood sugar levels in the immediate postoperative period as a guide for management has been sufficiently stressed.

SUMMARY

Five cases of hyperinsulinism are reported. In 2 cases a benign tumor was found; in 2 tumor was not found, but an excellent result was obtained by subtotal resection of the pancreas. In 1 case there was carcinoma with metastases to the lymph nodes, with recurrence after resection of all visible and palpable diseased tissue.

The criteria for a diagnosis of an islet cell tumor are stressed, as is the importance of operation when these features are present. The necessity for a careful exploration of the total gland at operation is likewise stressed.

APPENDICITIS

A Ten Year Survey: 1935 Through 1944

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APPENDICITIS is still a very prevalent disease, and there are still many problems in the treatment which have not been conclusively solved. The accumulation and the reporting of the experience in the treatment of adequately large groups of patients will record the trend of thought and management as well as assist in forming conclusions helpful in the treatment of appendicitis. It is for that purpose that this report is made concerning the treatment of appendicitis in St. Joseph's Mercy Hospital, Ann Arbor, Mich., during the ten year period 1935 through 1944. This period was chosen because the first five years represent the introduction of intravenous fluids, continuous gastric suction, more frequent blood transfusions and certain changes in surgical technic. The second five years had the added advantages of the sulfonamide compounds, but penicillin was not yet used. These two periods lend themselves to certain comparisons as to methods of treatment and results.

In this study are included the cases of all patients treated for appendicitis or for whom appendectomy was done as a primary operation during this ten year period. Any statistical study is as reliable as the records on which it is based. For this purpose, it is fortunate that St. Joseph's Mercy Hospital has a closed staff. Although a total of nineteen surgeons performed appendectomies during this ten year period, six did 95 per cent of the total operations and three of these did 75 per cent of the total. Operative notes were dictated by the operating surgeon, and the records have been well kept, except during 1944, when the war curtailed the staff. The attitude of the staff has been one of conservatism toward innovations. Unfortunately, during 1935 through 1937, there were still some patients who were being treated without the benefit of intravenous fluids and gastric suction. Sulfonamide compounds were little used before 1941. Early ambulation was not practiced during the period studied. Changes were adopted only when proved by experience elsewhere. The vast majority of the patients treated came from the

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immediate vicinity and must be considered as private patients, although occasionally their care was financed by the county welfare funds.

During the ten year period of study (1935 through 1944) 2,179 patients were treated for appendicitis. This comprised 4 per cent of all patients admitted during this period, and the operations constituted 8 per cent of all major surgical procedures.[1] Of the total group, 913, or 41 per cent, were classified as having recurrent or interval appendicitis, and they will not be referred to again in this paper, except in the matter of correlating the clinical problem with the pathologic findings. There was no mortality in that group. A group of 1,266 patients were treated for suppurative appendicitis, with an over-all mortality of 1.9 per cent; but, of these, 225 either had no microscopic evidence of suppurative appendicitis or had another disease which was found at operation. There were 2 fatalities. This leaves 1,042 patients treated correctly for suppurative appendicitis, with an over-all mortality of 2.1 per cent. In the discussion of treatment, the mortality statistics will be adjusted to

TABLE 1.—*Classification of 2,179 Cases of Appendicitis in Which Treatment Was Given: 1935-1944*

Classification	Cases		Mortality, %
	No.	%	
Recurrent appendicitis	913	41.9	0
Suppurative appendicitis	1,042	47.7	2.1
Unsubstantiated diagnosis	225	10.0	0.1

eliminate figures for patients who received no treatment, owing either to their critical condition or to an error in diagnosis.

All operative material was examined by the pathologist. The terminology of the pathologist may be misleadingly polite, or he may honestly wish to admit that there may be clinical symptoms unexplained by microscopic changes. Because there may be described microscopically in an appendix many changes which must be interpreted with caution in view of the expected wear and tear of time, for the purpose of this paper only those with the minimum criterion of acute suppurative appendicitis with purulent exudate in the lumen and pyogenic infiltration of the wall were included under the heading of acute appendicitis. This eliminated cases of the sort reported as catarrhal appendicitis, active chronic appendicitis, acute exacerbation of chronic appendicitis, mechanical appendicitis and others. These cases were placed in the group of interval or recurrent appendicitis. This is a very rigid classification and undoubtedly helps to account for a high percentage of error in diagnosis. However, it places the cases included in this report beyond

1. McCullough, J. Y.: Survey of Some Aspects of Appendicitis, Ann. Surg. **75**:453 (March 4) 1948.

question. A combination of the clinical picture presented by the patient, the operative findings described by the surgeon and the report of the pathologist was used to make the diagnosis of appendical abscess or peritonitis of appendical origin. Most authors [2] classify their reported cases as instances of (1) simple acute appendicitis, (2) peritonitis of appendical origin and (3) appendical abscess. Only a few authors [3] have expressed the belief that it is possible to separate the cases of localized peritonitis from those of generalized or spreading peritonitis. During the period studied by this report, the staff of this hospital thought that the clinical picture of generalized peritonitis was clearcut enough to warrant that diagnosis. Spreading peritonitis, indicating a progressive condition, was a diagnosis made only afer the clinical course of the patient showed it to be so. The observations of the pathologist have occasionally been used as the basis for classification.[4]

In the detailed discussion of treatment, localized peritonitis of appendical origin will be differentiated from generalized peritonitis,

TABLE 2.—*Classification of 1,042 Cases of Proved Appendicitis: 1935-1944*

Classification	Cases		Mortality, %
	No.	%	
Acute appendicitis	771	73.9	0.1
Appendical peritonitis	219	21.0	7.3
Appendical abscess	52	4.9	9.6

but for general purposes of discussion the 1,042 cases are classified as follows (table 2): (1) 771 cases of acute appendicitis in which the disease was localized to the appendix; (2) 219 cases of appendical peritonitis in which at operation there were cloudy fluid and purulent exudate on the surrounding organs or in which the clinical picture was that of a severely ill patient, giving a history compatible with appendicitis and presenting the signs of generalized peritonitis, and (3) 52 cases of appendical abscess.

2. (*a*) Reid, M. R.; Poer, D. H., and Merrell, P.: A Statistical Study of 2,921 Cases of Appendicitis, J. A. M. A. **106**:665 (Feb. 29) 1936. (*b*) Miller, E. M.; Fell, E. H.; Brook, C., and Todd, M. C.: Acute Appendicitis in Children, J. A. M. A. **115**:1239 (Oct. 12) 1940. (*c*) Green, H. W., and Watkins, R. M.: Appendicitis in Cleveland, Surg., Gynec. & Obst. **83**:613 (Nov.) 1946. (*d*) Meyer, K. A.; Requarth, W. P., and Kozoll, D. D.: Progress in the Treatment of Acute Appendicitis, Am. J. Surg. **72**:830 (Dec.) 1946. (*e*) Hoerr, S.: Factors in the Reduction of Mortality of Appendicitis, Surgery **22**:402 (Aug.) 1947. (*f*) Strohl, E. L., and Sarver, F. E.: Acute Appendicitis, Arch. Surg. **55**:530 (Nov.) 1947.

3. (*a*) Barrow, W., and Ochsner, A.: Treatment of Appendical Peritonitis, J. A. M. A. **115**:1246 (Oct. 12) 1940. (*b*) Ochsner, A., and Johnston, J. H.: Appendical Peritonitis, Surgery **17**:873 (June) 1945.

4. Jennings, J.: Burger, H., and Jacobi, M.: Acute Appendicitis: A Clinical and Pathological Study of 1,630 Cases, Arch. Surg. **44**:896 (May) 1942.

There have been many series of cases reported in the literature.[5] Up to the middle 1930's, there was a slow, but steady, decrease in the mortality from appendicitis. In the last ten years, there has been a sharp decrease in the mortality. The possible variables have been carefully analyzed many times to find the secret of success, but usually it has been hard to credit any one factor.[6] However, early diagnosis and immediate operation obviously constitute the potential factors making for a perfect record, as the mortality in the first twenty-four hours of the disease is negligible. If there is a significant reduction in the time before operation and therefore in the percentage of complicated cases, an improvement in the mortality may be expected. Also, the role of the sulfonamide compounds and penicillin may be important.

TABLE 3.—*Variation in Annual Distribution and Mortality*

	Acute Appendicitis		Appendicitis with Localized Peritonitis		Appendicitis with Generalized Peritonitis		Abscess		Totals		
Year	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	%
1935.....	36	0	19	0	0	0	3	3	58	2	3.4
1936.....	48	1	15	3	2	1	2	0	67	5	7.4
1937.....	65	0	11	0	0	0	7	1	83	1	1.2
1938.....	89	0	16	1	2	0	5	2	112	1	0.8
1939.....	70	0	16	0	5	1	7	0	98	3	3.0
1940.....	98	0	30	3	2	0	6	0	136	3	2.2
1941.....	111	0	18	0	3	0	3	0	135	0	0.0
1942.....	123	0	21	1	7	2	5	0	156	3	1.9
1943.....	80	0	21	1	6	3	5	0	112	4	3.5
1944.....	51	0	22	0	3	0	9	0	85	0	0.0
Total.....	771	1	189	9	30	7	52	5	1,042	22	
Mortality.....	0.1%		4.7%		23.3%		9.6%		2.1%		

It must be remembered that the improvement was being noted before sulfonamide drugs were used. Before I present my impressions of the significance of early diagnosis, short time interval before operation, age, incisions, drainage and the sulfonamide drugs, it would be well to consider the variations in annual distribution and mortality (table 3). It can be seen that near perfection was achieved during 1937 and 1938; hence a report based on these two years would have been optimistic. Also, in 1941 there were 135 consecutive cases without a death; actually, 175 cases were observed before a death occurred, during 1942. This

5. Schullinger, R.: Observations on Mortality from Acute Appendicitis at a University Hospital, 1916-1946, Ann. Surg. **126**:448 (Oct.) 1947. Jennings, Burger and Jacobi.[4]

6. (*a*) Hoerr, S.: Mortality Factors in Acute Appendicitis, Surgery **18**:205 (Sept.) 1945. (*b*) Zinninger, M., and Taskiro, S.: Appendicitis: A Review of Nine Hundred and Thirty-Six Cases at the Cincinnati General Hospital, Arch. Surg. **53**:545 (Nov.) 1946. (*c*) Green and Watkins.[2c] (*d*) Meyer, Requarth and Kozoll.[2d] (*e*) Hoerr.[2e]

fact is mentioned to emphasize the weakness of any conclusion based on a yearly report.

DELAY IN HOSPITALIZATION

Delay in hospitalization, or the time interval from the recorded onset of symptoms to admission to the hospital, has frequently been emphasized. As many authors have pointed out, if the operation occurs before the disease has extended beyond the appendix the mortality will be negligible. Statistical analyses giving the average number of hours before admission are of interest and have been used as an indication for operation or conservative treatment.[3a, b] If a significant reduction has been made, progress is undoubtedly being made, but the truly important factor is: In what stage of the disease was the patient admitted to the hospital? If there is a significant reduction in the number of complicated cases, the mortality will fall. Unfortunately, as many authors [7] have pointed out, peritonitis may occur very quickly in the clinical course of the disease. There was no improvement to report in the two five year periods studied. During the years 1935 to 1939, 26.1 per cent of the patients had evidence of peritonitis or abscess and 25.9 per cent during 1940 to 1944. Almost half of the cases of localized peritonitis and a third of the cases of generalized peritonitis occurred within twenty-four hours of the recorded onset of symptoms. However, it is significant to note that no deaths occurred in patients operated on within twenty-four hours of the onset of symptoms. Among those operated on from twenty-four to forty-eight hours after the onset of symptoms there was a 4.4 per cent mortality and an 8.4 per cent mortality among those operated on after three days.

PROBLEMS OF DIAGNOSIS

The relative importance of the various symptoms, physical signs and laboratory data in the diagnosis of appendicitis has been described many times. There would seem to be no reason for an error in diagnosis or delay in treatment once the patient has reached the hospital. Unfortunately, this is not so. In addition to those rare cases in which the diagnosis is not made until late in the disease or until autopsy, there is a significant group in which the diagnosis is in doubt on admission and may still be in doubt at operation. Zinninger [6b] found only 61 per cent of patients presented the classic picture of appendicitis. In this series 92 per cent of patients with proved acute appendicitis had either a reasonably typical history or physical findings. Operation was delayed in 6.2 per cent for further study with no recorded detriment to the patient. Of 189 cases of localized appendical peritonitis, operation was delayed in 6.8 per cent for further study, with probable detriment to 3 patients; this delay may have been a contributing factor to the death of another. A

7. Jennings, Burger and Jacobi.[4] Zinninger and Taskiro.[6b]

delay of several hours in an atypical case for a second examination, recheck of the laboratory work or consultation will seldom do harm and may prevent unnecessary operations. This attitude in no way excuses the missed diagnosis. However, the benefits of immediate operation have been so emphasized that in some communities, the patient need only mention discomfort in the right side to find himself the victim of an emergency operation. Granted that there is no excuse for delaying an operation that is indicated, it would still be a good thing if at hospital staff meetings the report of the pathologist could be checked for all appendixes removed at an emergency operation. As previously mentioned, the correlation of the clinical picture and the findings of the pathologist is still to be clarified. Jennings, Burger and Jacobi [4] have shown that there is little correlation between the clinical signs and symptoms and the pathologist's findings. They report perforation after only six hours of illness. In this series, we have taken acute suppurative appendicitis with purulent exudate in the lumen and pyogenic cellular infiltration of the wall as the minimal criterion for the clinical diagnosis of acute appendicitis. This is a very rigid classification and, perhaps, should be considered in the error in diagnosis. Of 1,229 patients operated on for suppurative appendicitis, 187 did not have the microscopic evidence previously mentioned. Of these 187 patients 149 were operated on as presenting true emergencies and 38 only after delay for study. Eighty-one per cent of these gave either a satisfactory history or had physical findings typical of appendicitis. There was 1 fatality, the patient dying with the signs and symptoms of generalized peritonitis on the fourth postoperative day. Either the pathologist reported on the wrong appendix and this was a true case of suppurative appendicitis, or the stump, which had been buried, blew out. These 187 cases represent a 15 per cent error in diagnosis of acute appendicitis, which was fairly evenly distributed among the six surgeons doing 75 per cent of the operations. Perhaps this error is too high; however, this figure is not far from that of Jennings and associates,[4] who found 11.9 per cent unsubstantiated diagnoses. Furthermore, of considerable interest is the fact that of the 994 patients operated on for recurrent appendicitis, 81 had acute suppurative appendicitis. This was an 8 per cent error and probably only helps to confuse the problem in the correlation of the clinical picture with the observations of the pathologist. There was no significant difference in the two five year periods studied.

The differential diagnosis between acute appendicitis and other abdominal conditions has been outlined many times. However, as is shown in table 4, other abdominal diseases were encountered in patients with a preoperative diagnosis of acute appendicitis.

Mistakes in diagnosis were made for 38 patients, or 3 per cent of those operated on for acute appendicitis. In only 4 instances was opera-

tion mandatory: in the cases of acute Meckel diverticulitis and volvulus of the ileum. More thorough study would certainly have eliminated the operations for genitourinary conditions and for pregnancy. The other 20 patients whose disease originated in the pelvis, theoretically should not have been operated on; but, practically, this is probably not a bad range of error. There were no significant differences in the two five year periods. There was 1 fatal case, that of a patient with acute cholecystitis whose gallbladder was drained. Death occurred on the sixteenth postoperative day. Autopsy showed only a dilated right side of the heart.

INCISIONS

At the beginning of this study the right rectus incision was used almost exclusively. As the advantages of a muscle-splitting incision in the right lower abdominal quadrant were recognized, the right rectus incision was largely discarded, except by one operator. Although this change occurred as the mortality was being lowered, the improvement

TABLE 4.—*Classification of 38 Cases not Acute Appendicitis*

Pelvic		Genitourinary		Gastrointestinal		Miscellaneous	
Ruptured follicle	11	Urinary tract infection	4	Meckel's diverticulitis	3	Toxic psychosis	1
Acute salpingitis	8	Sulfonamide crystalluria	1	Acute cholecystitis	3	Peritonitis following chickenpox	1
Chronic salpingitis	1	Hydronephrosis	1	Volvulus of ileum	1		
Pregnancy	2	Perirenal abscess	1				
Total	22		7		7		2

took place among the complicated cases, in which there were other factors, probably of more importance than the incision. Despite the benefits credited to the McBurney incision by other authors,[8] it is hard to evaluate properly the incision used in this series, except as to morbidity. The right rectus incision was consistently associated with an average hospital stay of fourteen plus days, whereas, in contrast, the McBurney or Davis incision necessitated slightly less than seven days.

DRAINAGE

When to drain has always been a controversial point. Schullinger [5] has again repeated the principles of drainage, which are, in short: to drain actual purulent fluid, to drain areas in which there is necrotic tissue and to drain clean areas that have been opened to infection. There has been a marked tendency in recent years not to drain but to let the peritoneal cavity take care of the infection.[9] Certainly the

8. Reid, Poer and Merrell.[2a] Strohl and Sarver.[2f] Jennings, Burger and Jacobi.[4] Schullinger.[5] Zinninger and Taskiro.[6b]

9. Jackson, A.: Early Ambulation in Cases of Perforated Appendicitis, Arch. Surg. **54**:644 (June) 1947. Meyer, Requarth and Kozoll.[2d]

morbidity is greatly reduced by primary peritoneal closure unless a secondary abscess occurs. Zinninger [6b] has warned against too frequent closure, as he found an increase in intra-abdominal abscess in a more recent series of cases reported. In this series, a change of policy occurred suddenly in 1939. Prior to that time drainage was instituted in 18 per cent of the cases of acute appendicitis; subsequently, in only 3 per cent. In 6 cases pelvic abscesses occurred, in 4 despite drainage. Prior to 1939, drainage was instituted in 91 per cent of the cases of localized peritonitis. Subsequently, only 50 per cent, and during the last year of this study, only 33 per cent were drained. One abscess in the right lower quadrant and 1 subphrenic abscess occurred despite the usual type of drainage. One abscess in the right lower quadrant occurred after primary peritoneal closure. All appendical abscesses operated on were drained. This small incidence of secondary intra-abdominal abscess, occurring mainly despite drainage, seems clearly to indicate that the increase of primary peritoneal closure had

TABLE 5.—*Age Distribution*

Years	No. of Cases	% of Complicated Cases	No. of Deaths*	Mortality Rate, %
0-9	76	50	2	2.6
10-49	858	15	4	0.4
50-59	53	64	6	11.0
60-69	31	74	4	12.0
70-79	5	100	4	80.0
80	1	100	1	100.0

* Age unknown for 1 death.

been done without harm to the patient and should continue. Wound drainage alone was frequently done in cases in which there had been contamination of the wound. This was either as a delayed closure technic or as drainage to the peritoneum.

The fact that in all fatal surgical cases drainage had been instituted only indicates the seriousness of the patients' condition rather than discrediting drainage. It also shows that primary peritoneal closure when used did not contribute to the mortality. Drainage will still be used when there is something localized to drain. This will mean appendical abscesses and many cases of peritonitis.

AGE

Appendicitis in the very young and in the advanced age group has been shown to carry a high mortality.[4] The symptoms and clinical findings are less typical, and the patients are less able to withstand surgical procedures. Also, peritonitis will have occurred more frequently by the time of operation. In this series, the mortality among the patients over 60 years of age was extremely high (24 per cent),

emphasizing the problem of surgery in the aged. Table 5 shows the age distribution, per cent of complicated cases and mortality. The greatest incidence was in the decade 10 to 19 years (292 cases) and the next greatest in the 20 to 29 year group (256 cases).

There was no significant difference in the age incidence in the two five year periods studied.

CONSERVATIVE TREATMENT

As stated earlier in this report, the consensus of this staff has been that the diagnosis of generalized peritonitis can be made in contrast to that of localized peritonitis. The diagnosis of appendical abscess seems to have been more difficult to make. The selection of cases for conservative treatment has depended on the individual surgeon's opinion. Conservative treatment for generalized peritonitis and abscess was started in this hospital in 1938. Since that time, it has had a definite place in the management of these conditions, particularly in the critically ill. However, conclusions drawn from such a small series of cases as this series must be carefully considered.

Of 189 patients with localized peritonitis 187 were operated on; hence conservative treatment was not used. Of 30 patients with generalized peritonitis, the cases of 27 are suitable for study. Two patients died before treatment could be started, and a diagnosis was not made until autopsy in the third case. Of these 27 remaining patients, 13 were operated on, with 3 deaths from peritonitis. Fourteen patients were treated conservatively, with 1 death, that of an elderly patient with diabetes associated with cardiovascular disease who was not considered fit for operation during the sixteen days of his hospital stay.

There were 52 cases of appendical abscess. Fifty only are suitable for study, as 1 patient was considered too ill for any treatment and the diagnosis was not made until autopsy in the second case. Thirty patients were operated on, with 2 deaths. Drainage alone (used in 17 patients, with no deaths) was done unless the appendix was readily available. In 5 cases, the abscess was not suspected preoperatively, and in 2 additional cases, the preoperative diagnosis was that of a pelvic condition. More accurate diagnosis would have reduced the number of persons operated on. Twenty patients were treated conservatively, but 5 subsequently required drainage of the abscess, with 1 fatality. Conservative treatment for generalized peritonitis and appendical abscess was certainly followed by no greater mortality than was immediate operation. Because of the tendency to use conservative treatment for critically ill patients, it should receive more credit in the reduction of the mortality than the statistics would indicate. Although conservative treatment was not used until 1938, statistically it was used equally in the two five year periods.

THE SULFONAMIDE COMPOUNDS

The sulfonamide compounds were not used until late in 1940 and were not used adequately until 1941. They were never used to any great extent in simple acute appendicitis, the peak of popularity being in 1942 with 10 per cent of the cases. Consistently, 50 per cent of the patients with localized peritonitis have received these drugs since 1940. In the 4 fatal cases suitable for study, 2 patients received adequate sulfonamide therapy, 1 was inadequately treated and 1 received no sulfonamide drugs. Eighty-five per cent of the patients with generalized peritonitis have received these drugs since 1940. Of 3 patients who died, 2 received adequate amounts of sulfonamide compounds and 1 received none. Seventy-seven per cent of the patients with abscess received adequate sulfonamide therapy. There were no deaths.

There have been many reports concerning sulfonamide treatment of appendicitis.[10] Its routine use has been advocated, and much improvement has been credited to its use. However, the routine use of sulfonamides will not eliminate all complications or deaths from appendicitis, and physicians who expect them to do so will certainly be disappointed. For the complicated cases—that is, of abscess and peritonitis—sulfonamide therapy certainly has been accepted. This small series of cases tends to show that sulfonamide compounds will not prevent death from appendicitis but must be given much of the credit for reducing mortality. Penicillin and streptomycin are now being evaluated.

MORTALITY

The cause of death has been studied carefully by many authors and has been reported in most articles.[11] Peritonitis, ileus and undrained abscesses are the commonest causes. Table 6 shows the causes of death in this series.

Generalized peritonitis is the most common. Of the 10 such cases treated, 9 occurred in the period 1935-1939, which would indicate that postoperative generalized peritonitis has almost been eliminated as a cause of death among patients treated in 1940-1944 and is a major

10. (*a*) Ravdin, T.; Rhoades, J., and Lockwood, J.: The Use of Sulfanilamide in the Treatment of Peritonitis Associated with Appendicitis, Ann. Surg. **111**:53 (Jan.) 1940. (*b*) Stafford, C.; Beswick, J., and Debb, P. H.: Evaluation of Sulfonamides in the Treatment of Peritonitis of Appendiceal Origin, Am. J. Surg. **64**:227 (May) 1944. (*c*) Aycock, T., and Farris, E. M.: The Possible Effects of Sulfonamides on the Mortality of Appendicitis, Ann. Surg. **121**:710 (May) 1945. (*d*) Mueller, R.: The Local Use of Sulfonamides in the Treatment of Acute Appendicitis, Ann. Surg. **122**:625 (Oct.) 1945. (*e*) Griffin, W.; Silverstein, H.; Hardt, H., and Seed, L.: Prophylactic Chemotherapy in Appendicitis, J. A. M. A. **133**:907 (March 29) 1947.

11. Green and Watkins.[2e] Schullinger.[5] Hoerr.[6a]

factor in the improvement in mortality in this period. There is, of course, no excuse for the failure to make a diagnosis in 2 cases until autopsy or for the postoperative subphrenic abscess, which was allowed to perforate into the lung. Little could have been done to prevent the deaths from coronary occlusion and pulmonary embolism. A more optimistic or energetic attitude might have saved the 4 elderly patients who were considered either too feeble to withstand operation or who were allowed gently to pass on.

In evaluating the effect of treatment on the mortality statistics, it would seem reasonable to eliminate from consideration those patients who received no treatment, either because they were moribund on admission (2 cases) or because no diagnosis was made until autopsy

TABLE 6.—*Causes of Death*

	1935-1939	1940-1944
Generalized peritonitis	9	3*
Age and cardiovascular disease	1	3
No diagnosis	1	1
Undrained subphrenic abscess	0	1
Coronary occlusion	0	2
Pulmonary embolism	0	1

* 2 patients moribund on admission.

TABLE 7.—*Results of Treatment on Mortality Statistics*

	Acute Appendicitis			Localized Peritonitis			Generalized Peritonitis			Abscess			Totals		
	Cases, No.	Deaths, No.	%	Cases, No.	Deaths, No.	%	Cases, No.	Deaths, No.	%	Cases, No.	Deaths, No.	%	Cases, No.	Deaths, No.	%
1935-1939	308	1	0.32	77	4	5.2	9	2	22	23	4	17	416	11	2.6
1940-1944	463	0	0.0	112	5	4.4	18	2	11	28	0	0.0	622	7	1.1

(2 cases). The 2 patients with coronary occlusion and the 1 with pulmonary embolism were clinically well at the time of the complication. Autopsy showed a clean abdomen in 2, but these cases are included because the treatment may have influenced the occurrence of the fatal complication. There were no deaths attributed to anesthesia.

Table 7 shows the difference in the mortality statistics in the two five year periods studied, corrected as just outlined. The over-all mortality dropped from 2.6 to 1.1 per cent, which is significant. This was achieved by the great improvement in the results of the treatment of abscess and generalized peritonitis. In attempting to determine the reason for this improvement, the fact that generalized peritonitis was almost eliminated as a cause of death among the treated patients stands out. Undoubtedly, the use of sulfonamide drugs must be given the greatest credit for this change. Although the statistics do not prove it, there is the impression among the staff that conservative treatment has

done much to bring about this improvement. Other factors, such as age distribution, diagnosis, early operation and drainage, were not appreciably different in the two periods. The change from the right rectus incision to the muscle-splitting incision in the right lower quadrant is hard to evaluate. Undoubtedly, there is less chance of converting a localized peritonitis into a generalized peritonitis by the use of the lateral incision.

The results of treatment of appendicitis complicated with localized peritonitis were not encouraging. The sulfonamide compounds were used in only 50 per cent of the cases, but of the 5 deaths only 1 was due to peritonitis. Three were associated with cardiovascular conditions and 1 with faulty diagnosis. Although success may be attained in controlling postoperative peritonitis, further improvement will require more successful treatment of the problems of the aged.

CONCLUSIONS

A survey of the treatment of appendicitis at St. Joseph's Mercy Hospital during 1935-1944 has shown an improvement. This was obtained mainly in those cases of appendical abscess and generalized peritonitis treated during the second five year period. The reduction in postoperative generalized peritonitis as a cause of death would indicate that the use of sulfonamide drugs deserves much credit. However, 4 deaths were recorded, despite adequate sulfonamide therapy. Conservative treatment is the second factor which has favorably influenced the results. To improve results still further, more adequate treatment must be directed toward the problem of the aged and more accurate diagnosis must be obtained.

SUMMARY

The treatment of appendicitis in St. Joseph's Mercy Hospital, Ann Arbor, Mich., during a ten year period, 1935 to 1944, is reviewed. During this time, 2,179 patients were treated primarily for appendicitis, of whom 41.9 per cent were treated for interval appendicitis, 47.7 per cent for proved suppurative appendicitis and 10.4 per cent with the diagnosis of appendicitis unsubstantiated.

Improvement was noted in the second five year period. The variable factors are reviewed to determine the cause of this improvement. The incidence of complicated cases was 26.1 per cent in 1935 to 1939, which was approximately the same as that of 25.9 per cent in 1940 to 1944. The interval of time from onset of symptoms to operation was not improved. The higher mortality in advanced age groups is again pointed out. The age distribution was the same for the two periods. The use of drainage was greatly curtailed, without harm to the patient and with a great improvement in the morbidity but probably little effect

on the mortality. The right rectus incision was largely abandoned for the muscle-splitting incision in the right lower quadrant, but this change could not be adequately evaluated. The problems of diagnosis are discussed from the standpoint of the correlation of the pathologist's report with the clinical picture. On the basis of a very rigid standard to confirm the diagnosis of acute appendicitis, it was found that 15 per cent of the patients operated on did not have appendicitis. The other abdominal conditions encountered are listed. Although more accurate diagnosis could greatly improve the results, this was not a factor in the improvement of the mortality. In reviewing the causes of death, it is noted that postoperative generalized peritonitis was almost eliminated as a cause of death during the second five year period. The use of the sulfonamide drugs was given the major share of the credit for this, with the conservative treatment of abscess and peritonitis a contributing factor. To improve results still further, more accurate diagnosis and more effective treatment of the aged are needed.

A third five year report covering the years 1945 to 1949 will be presented to evaluate the addition of penicillin to the treatment of appendicitis.

TETRAETHYLAMMONIUM CHLORIDE IN EXPERIMENTAL VASCULAR INJURIES OF LIMB, BOWEL AND HEART

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DETROIT

IN THEIR study of quaternary ammonium compounds, Burns and Dale [1] found that tetraethylammonium chloride (TEAC) had a nicotine-like action but was void of either a curare-like or muscarine-like action. The more recent studies of Acheson and Moe [2] showed the action of tetraethylammonium chloride to be one of blockade of the cholinergic ganglions of the sympathetic and parasympathetic nervous systems. After administration of tetraethylammonium chloride the effects of preganglionic stimulation are abolished but not the effects of postganglionic stimulation or of drugs with a peripheral action. According to Loewi,[3] the mechanism of autonomic blockade by tetraethylammonium chloride still remains to be explained.

The generalized autonomic ganglion blockade produced by this drug results in a transient fall in systemic blood pressure and an increase in both peripheral blood flow and skin temperature. These effects, due to the removal of vasoconstrictor tone by action on the sympathetic ganglions, suggested the use of the drug in peripheral vascular disease, such as Raynaud's phenomenon, Buerger's disease, causalgia, reflex dystrophy, thrombophlebitis, trench foot and immersion foot.

One objective of the present study was to determine whether establishment of collateral circulation following experimental injury to a major blood vessel, such as the femoral artery, would be enhanced

From the Experimental Surgical Laboratory, Harper Hospital.

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1. Burns, J. H., and Dale, H. H.: J. Pharmacol. & Exper. Therap. **6**:417, 1914-1915.

2. Acheson, G. H., and Moe, G. K.: J. Pharmacol. & Exper. Therap. **84**:189, 1945; ibid. **87**:220, 1946.

3. Loewi, O.: J. Pharmacol. & Exper. Therap. **88**:136, 1946.

by the use of tetraethylammonium chloride. For this purpose we ligated and sectioned the abdominal aorta in dogs and followed the clinical course in both untreated control animals and animals treated with tetraethylammonium chloride. This procedure was thought suitable for our purpose, since Leriche [4] found that the ultimate result of the operation was death from gangrene of the hindlimbs in about seventy-two hours and Mulvihill and Harvey [5] had shown that a generalized reflex vasospasm occurs in collateral vessels when an artery is ligated. Prevention of cyanosis, paralysis and gangrene of the limb and death of the animal could be taken as evidence of the efficacy of tetraethylammonium chloride in preventing reflex vasospasm. While this study was in progress, Cooper, Robertson and Dennis [6] published their results of a similar study with essentially similar findings.

Most of the vascular studies with tetraethylammonium chloride have dealt with the blood supply to the somatic structures, and little is known about its action on the blood vessels supplying the visceral organs. We therefore also undertook some experiments to determine the effects of the drug on the mesenteric and coronary blood vessels. It occurred to us that if the reflex vasospasm usually associated with arterial constriction could be reduced in intestinal and coronary vessels the drug might prove of value in the treatment of mesenteric thrombosis and the anginal syndrome.

PROCEDURES

The experiments were carried out on healthy mongrel dogs weighing 15 to 20 pounds (6.8 to 9.1 Kg.). All operations were performed after the animals had been fasted for twenty-four hours; pentobarbital sodium was given intravenously as the anesthetic. Tetraethylammonium chloride [7] was given in nontoxic doses [8] either intramuscularly, 25 mg. per kilogram of body weight, or intravenously, 5 to 6 mg. per kilogram of body weight.

Ligation of the Abdominal Aorta.—These experiments were conducted on 29 dogs. The abdominal aorta was ligated just below the inferior mesenteric artery and above the bifurcations. The aorta was then divided between the ligatures, preventing reformation of the continuity of lumen. The circumflex iliac arteries, direct branches from the aorta just below the inferior mesenteric artery, were also ligated, since these form an important source of blood supply to the lower extremity. This origin is in contrast to that in the human being, in whom these vessels are branches of the internal iliac artery.

4. Leriche, R.: Surgery of Pain, Baltimore, Williams & Wilkins Company, 1939.

5. Mulvihill, D. A., and Harvey, S. C.: J. Clin. Investigation **10**:423, 1931.

6. Cooper, F. W.; Robertson, R. L., and Dennis, E. W.: Surgery **22**:740, 1947.

7. The preparation used was etamon,® supplied through Dr. E. C. Vonder-Heide, of the laboratory of Parke, Davis & Company, Detroit.

8. Gruhzit, O. M.; Fisken, R. A., and Cooper, B. J.: J. Pharmacol. & Exper. Therap. **92**:103, 1948.

Of the 29 dogs operated on, 14 were used as a control series and were given no tetraethylammonium chloride after operation. The remaining 15 dogs were treated with the drug, starting immediately after ligation of the aorta. These animals were given 25 mg. of tetraethylammonium chloride per kilogram of body weight intramuscularly twice a day, always in the foreleg, because circulation in the hindleg is impaired and absorption is delayed. The drug was continued for three to seven days, with an average of four days. Treatment with the drug was stopped when the dog exhibited no symptoms of weakness or paralysis. No dog was treated for more than seven days.

The presence or absence of collateral vessels was demonstrated in both series of dogs by postmortem arteriograms, with use of a thin solution of barium, acacia and glycerine for injection into the thoracic aorta.

Studies on the Normal Stomach and Intestine.—Fluoroscopic and roentgen studies of the stomach and small bowel were made on unanesthetized dogs after administration of barium sulfate by stomach tube. After control observations of gastric peristalsis and gastric emptying of the barium meal, tetraethylammonium chloride was given intravenously in doses of 5 mg. per kilogram and roentgenologic observations continued.

Further studies on the small bowel were made by direct inspection of the exposed organ and by recordings of the serosal temperatures before and after administration of tetraethylammonium chloride, 5 to 6 mg. per kilogram. These studies were made on anesthetized animals, with use of intestinal loops. Serosal temperatures of the small bowel were recorded with a Rauh electrothermocouple. Temperature readings could be instantly made by applying the electrodes to the surface of the bowel. This was a distinct advantage when the response to a drug is as rapid as was the case with tetraethylammonium chloride. Preventing the drying of the serosal surface, controlling room air currents and gentle infrequent handling of the bowel were points which were considered important because any one might distort the normal temperature or normal state of the bowel. When these were standardized, the changes in the temperature readings were considered to result mainly from the drug effect.

Temperature readings were taken from the serosal surface of the small bowel after the loop had been delivered onto the abdominal wall and placed on moist sponges. The loop was treated the same way when normal curves were obtained or when curves after administration of tetraethylammonium were taken.

Twenty dogs were used and many temperature readings taken for both normal and tetraethylammonium chloride curves. In these cases the drug was given rapidly by the intravenous method in a dose of 5 to 6 mg. per kilogram.

Ligation of Superior Mesenteric Artery.—After the routine pentobarbital sodium anesthesia, the superior mesenteric artery was isolated and then ligated with heavy silk sutures in 7 dogs. Immediately after the ligation tetraethylammonium chloride was given intramuscularly and continued twice a day, using 25 mg. per kilogram of body weight. These injections were continued until the time of death.

Ligation of Smaller Mesenteric Vessels (Vasa Recti).—Sixteen dogs were used in this series of experiments. The vasa recti vessels of various lengths of bowel were ligated with fine sutures. To permit better comparison only the vasa recti in the ileum were used.

Eight pairs of dogs were used; 1 of each pair served as control, while the other was treated with 25 mg. of tetraethylammonium chloride per kilogram

of body weight three times a day. Eight different lengths of bowel, ranging from 3 to 8 cm., were deprived of their blood supply. All measurements were taken on the ileum after ligation and while the bowel was contracted.[9]

Experimental Strangulation of the Bowel.—The procedure of Laufman and Method[10] of constricting a segment of small bowel with umbilical tape was used. Segments of small bowel were ligated tightly enough to produce obstruction of venous return but still leave the smaller arcade arteries pulsating. After a period of thirty minutes to one hour the ligatures were released and the serosal temperatures were taken. To check the changes in the segment of bowel injured by the ligature, a normal segment of bowel several feet from the site of obstruction was used as a control. The serosal temperatures were recorded from the normal segment as well as from the portion of bowel previously under the effects of the vascular obstruction. These temperature readings were then repeated after administration of tetraethylammonium chloride.

Ligation of Coronary Vessels.—Using a transthoracic approach and positive pressure ventilation via an intratracheal tube, 6 dogs were operated on and the left descending or posterior coronary artery was ligated. Recovery was good, and clinically the animals exhibited no ill effects from the operation. Tetraethylammonium chloride was given intramuscularly, 25 mg. per kilogram twice a day. Electrocardiograms were taken at intervals to determine the effects of the operation and the treatment.

RESULTS

Effects of Tetraethylammonium Chloride Following Ligation of Abdominal Aorta.—After ligation of the abdominal aorta most of untreated dogs showed the typical paralysis of the hindlegs and evidence of impaired circulation as described by Leriche[4] and Cooper and co-workers.[6] The paralysis was not severe at first but progressed rapidly from coldness and cyanosis to a very evident gangrene of the hindlegs. Within twenty-four to seventy-two hours fatal gangrene developed; 11 of the 14 dogs died of either gangrene or ischemic paralysis. Three control dogs survived the operation but showed a moderate amount of paralysis for three to four days afterward. Thereafter, these 3 animals exhibited claudication in the posterior extremities for four to five weeks. This could be demonstrated by exercising the animals for five minutes. The hindlegs would become completly paralyzed and drag as the animals attempted to walk. However, when the dog was allowed to rest for ten to fifteen minutes, the paralysis disappeared and the strength and ability to walk returned. At the end of five weeks, these 3 animals showed no evidence of impaired circulation on exercise; possibly the collateral circulation was sufficient at this time to prevent these symptoms.

9. According to F. P. Mall (Johns Hopkins Hosp. Rep. **1**:1, 1896), 25 cm. of intestine will shorten to 15 cm. after ligation of the vasa recti. On this basis, the devascularized length of bowel measured in the relaxed condition, would range in our experiments from 5 to about 13 cm.

10. Laufman, H., and Method, H.: Surg., Gynec. & Obst. **85**:675, 1947.

In the group of 15 dogs operated on and treated with tetraethylammonium chloride, there was a marked absence of the paralysis, cyanosis and weakness of the posterior extremities so common in the control dogs. A few dogs showed a slight weakness and stiffness, but this was transient and disappeared after a few days of treatment. All but 4 animals of the treated group survived the operation and showed no residual or immediate effects from ligation of the abdominal aorta. They were able to stand and walk normally. No muscular impairment was noted in the hindlegs after exercise. Of the 4 treated dogs which died, in 2 gangrene of the hindlegs developed and 2 died of conditions unrelated to the experiment (distempter and peritonitis). It was observed that when an area of gangrene did develop, further

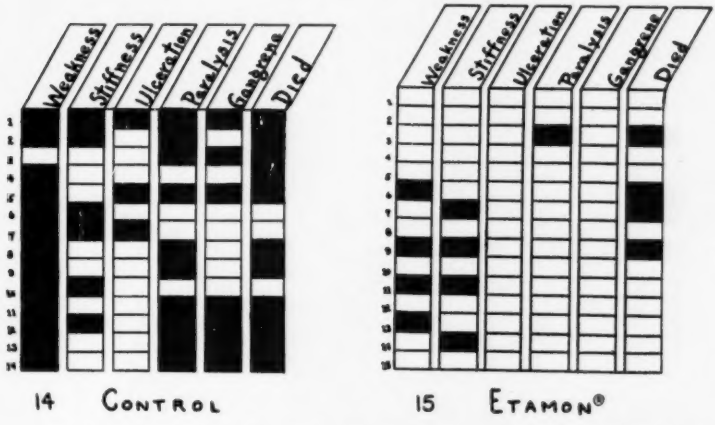

Fig. 1.—Complications in control and etamon®-treated dogs after ligation and division of the abdominal aorta. Each black rectangle indicates the presence of a particular symptom. More complications occurred in the untreated control group.

treatment with tetraethylammonium chloride was of no value in preventing extension of the process.

Figure 1 graphically contrasts the two groups of dogs by comparing the appearance of symptoms in each group. It is easily seen that many more symptoms and fatalities appeared in the control group than in the group treated with tetraethylammonium chloride. In figure 2, *A* and *B*, are arteriograms of control dogs showing the obstruction in the aorta produced at operation and the absence of the radiopaque material in the vessels of the lower extremity. In contrast to this, *C* is an arteriogram of a dog treated with tetraethylammonium chloride, killed five weeks after operation, in which the filling of the vessels of the posterior extremity is good.

Gross Effects of Tetraethylammonium Chloride on the Normal Stomach and Bowel.—After administration of 5 to 6 mg. of tetraethylammonium chloride per kilogram intravenously, peristaltic activity of the stomach was abolished. The concomitant gross changes observed in the loop of small bowel exposed on the abdominal wall were more marked and striking. This loop of small bowel became blanched and rippled and appeared to be in spasm. The description of "tiger stripes"

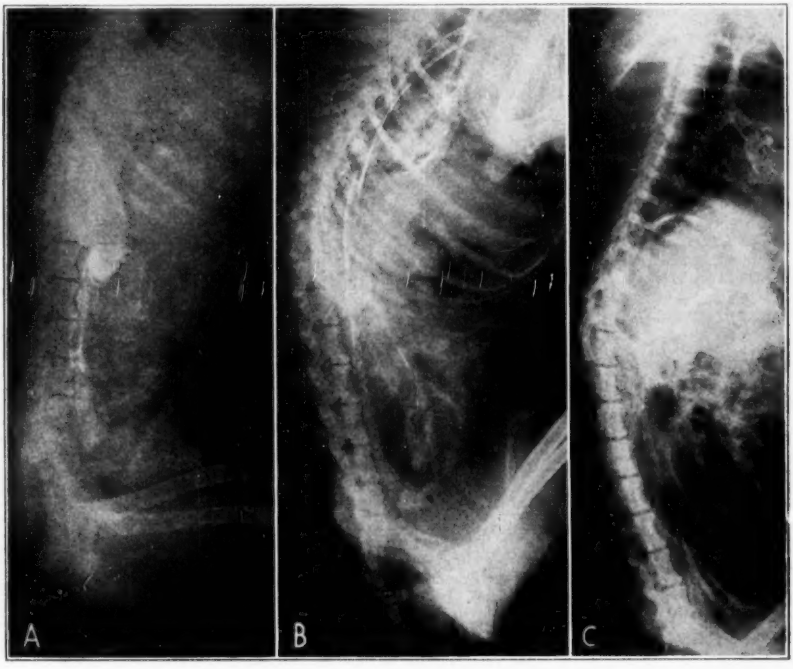

Fig. 2.—*A* and *B*, postmortem arteriograms of control dogs showing the obstruction in the aorta produced at operation and the absence of radiopaque material in the blood vessels of the hindlegs. Both of these animals died of gangrene of the hindlegs. *C*, postmortem arteriogram of an etamon®-treated dog showing the obstruction in the aorta produced at operation, and the abundant blood supply to the lower extremities when contrasted with *A* and *B*. This animal exhibited none of the complications so common in the control series and was killed for the arteriogram.

might fit the appearance of the bowel at this time. These effects lasted fifteen to twenty minutes. Thereafter feeble peristaltic waves began to go through this segment, and the pale appearance of the bowel soon gave way to its normal color.

Roentgenologic studies on unanesthetized dogs confirmed these findings obtained by direct inspection.

Effect of Tetraethylammonium Chloride on Serosal Temperature of Normal Bowel.—When the temperatures were recorded for a ten minute period from a loop of normal bowel, a slight fall, usually 1 to 3

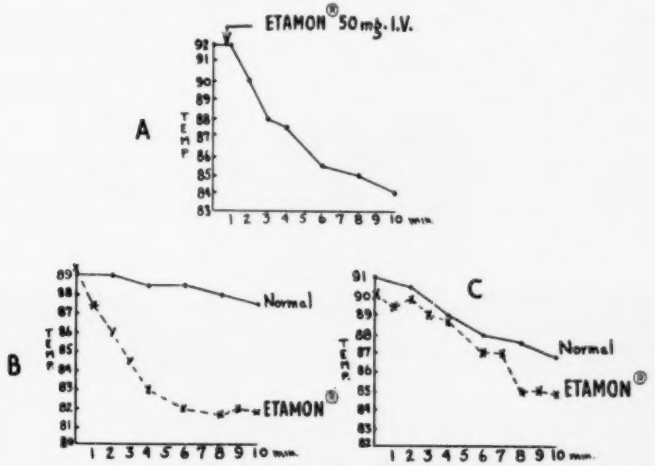

Fig. 3.—*A*, curve showing the typical rapid fall in the bowel temperature after administering etamon® intravenously and taking serosal temperatures at one minute intervals for ten minutes. *B* and *C*, curves showing the contrast between a normal ten minute curve and the same loop after administration of the drug.

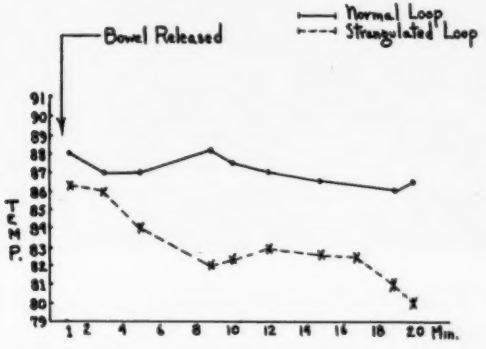

Fig. 4.—Curves showing the temperature responses in a 3 inch loop of normal bowel and a loop of bowel in which the venous return was obstructed for one hour. The fall in serosal temperature was greater in the strangulated loop of bowel.

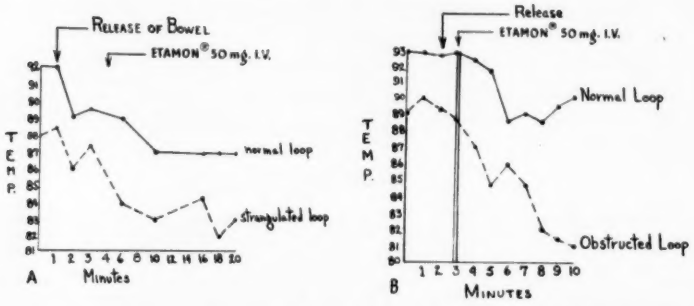

Fig. 5.—Temperature response in bowel after (*A*) sixty and (*B*) thirty minutes of venous obstruction and treatment with etamon® intravenously immediately after release of the venous obstruction. Etamon® had no effect as far as altering the serosal temperature was concerned.

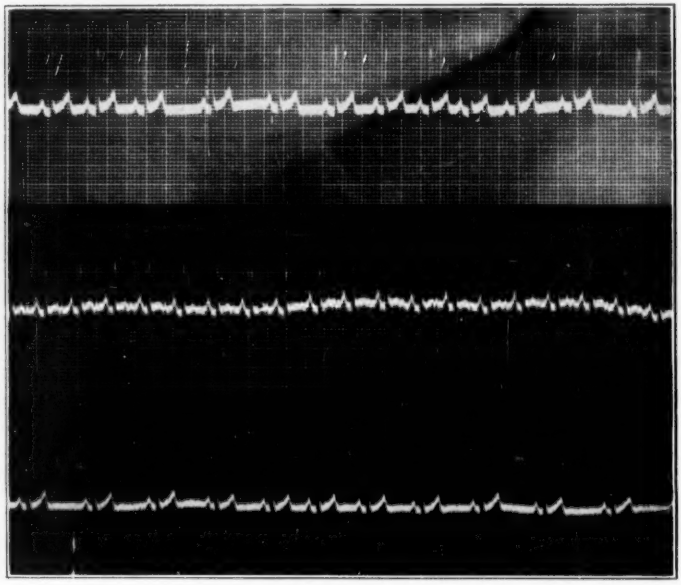

Fig. 6.—Electrocardiogram using normal leads taken on an anesthetized dog showing the effects of the intravenous administration of etamon® on a normal dog heart. The curve appears to be normal for a dog with marked sinus arrhythmia. After administration of etamon,® the rate became very rapid, approximately 155. The P and QRS complexes remained unchanged, but the T waves appeared to become flattened and then inverted. Fifteen minutes later the curve returned to normal.

degrees (F.), was obtained. This could be accounted for by exposure to room air.

When 5 to 6 mg. of tetraethylammonium chloride per kilogram of body weight was given rapidly intravenously, the change was immediate and marked. In every case, there was a marked fall in temperature, averaging 6 degrees. This drop continued for twenty to thirty minutes, reaching its lowest point in about ten minutes. Accompanying this drop in temperature, the appearance of rippling, spasm and blanching was seen in the bowel wall. Curve *A* in figure 3 shows a typical

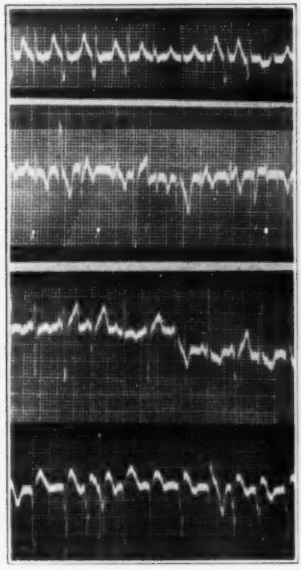

Fig. 7.—The left descending coronary artery was ligated and etamon® given intramuscularly. The electrocardiogram shows no axis deviation. The P-R interval is 0.12 second; the QRS complex, 0.06 second. There are periods of ventricular tachycardia during which P waves are seen acting independently of ventricular beats. The Q wave in lead I is large; the T wave in leads I and II deeply inverted. There are ventricular extrasystoles. The fourth lead shows typical acute coronary occlusion. The S-T segment is elevated, the T wave inverted and the QRS component normal. The diagnosis was acute anterior coronary thrombosis with runs of ventricular tachycardia.

rapid fall in the bowel temperature after administration of tetraethylammonium chloride; curves *B* and *C* show the contrast between a normal ten minute curve and the same loop of bowel after administration of tetraethylammonium chloride.

Effects of Tetraethylammonium Chloride After Ligation of the Superior Mesenteric Artery.—All animals died within twenty-four to thirty-six hours after operation and at autopsy showed massive gangrene of the small bowel and cecum. Prior to death these animals showed a bloody diarrhea. Treatment with tetraethylammonium chloride did not prolong the life of the animals, since in untreated animals Scott and Wangensteen [11] found the average survival time of dogs subjected to similar operation to be twenty hours.

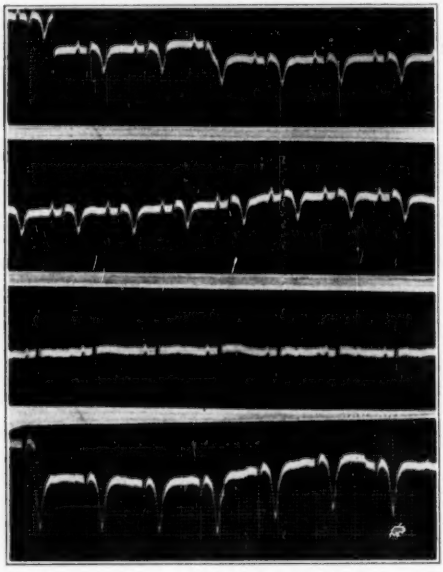

Fig. 8.—This electrocardiogram taken after ligation of the left descending coronary artery and administration of etamon® shows regular sinus rhythm and right axis deviation. The P waves are normal, the P-R interval 0.14 second and the QRS complex 0.05 second. There is no slurring, no R wave in lead I and very minute R waves in leads II and IV. The T wave in leads I and II is exaggerated and inverted, the T wave in lead II huge and inverted. There is some elevation of the segment in leads I, II and IV. There are no further ventricular extrasystoles. The diagnosis was acute anterior massive infarction.

Effects of Tetraethylammonium Chloride After Ligation of Smaller Mesenteric Vessels.—The immediate results of ligation of the vasa recti vessels were blanching of the bowel wall, cyanosis and development of areas of spasm. Ultimately the devascularized area became

11. Scott, H. G., and Wagensteen, O. H.: Proc. Soc. Exper. Biol. & Med. **29**:424, 1932.

gangrenous. Control dogs survived ligation of the vasa recti only if the bowel area involved was less than 5 cm. in length. When the ischemic area exceeded 5 cm. (measured along the mesenteric border after ligation) the inevitable outcome was gangrene, perforation of this segment and death from peritonitis. The administration of tetraethylammonium chloride did not affect the collateral circulation or the ultimate picture.

Effects of Tetraethylammonium Chloride After Strangulation of the Bowel.—In figure 4, the temperature responses of bowel when

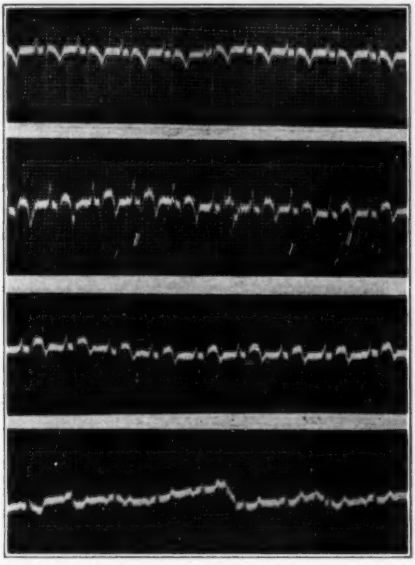

Fig. 9.—The left descending coronary arc was ligated twenty-four hours before the electrocardiogram was taken. The dog was active and its condition appeared good. The electrocardiogram shows regular sinus rhythm with groups of right ventricular extrasystoles in leads II and IV. The P wave is normal, the P-R interval 0.09 second, the QRS complex 0.05 second, without deformity. There is no R wave in leads I and II. The T wave in lead I is sharply inverted, in leads II and III diphasic and in lead IV erect. There is minimal elevation of the S-T segment in lead I and frank elevation and arching in leads II and III. The S-T segment in lead IV is somewhat depressed. The diagnosis was groups of right ventricular extrasystoles and acute posterior infarction.

no treatment was instituted after release of the bowel ligature are seen. It is noted that both the normal and the strangulated loops of bowel showed a fall in the serosal temperature. Figure 5 depicts the results in treated animals after the ligatures were released and

the bowel was relieved of the obstruction. As to dosage, 5 mg. of the drug per kilogram of body weight was used. The fall in temperature of the obstructed loop was greater than that of the control loop in every case, and tetraethylammonium chloride failed to alter the drop in serosal temperatures of either the strangulated or the control loops.

Effects of Tetraethylammonium Chloride Following Ligation of Coronary Vessels.—The effect of tetraethylammonium chloride on the electrocardiogram of the normal dog is shown in figure 6. This tracing was obtained by using normal leads. The dose of tetraethyl-

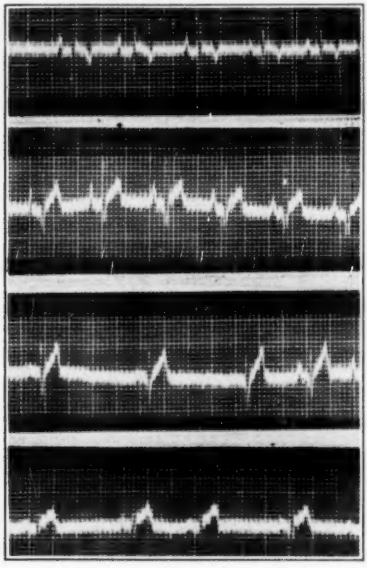

Fig. 10.—The coronary artery was ligated and etamon® given for six days. The dog's condition was very good. The electrocardiogram shows a variable sinus rhythm with stretches of bradycardia, with the auriculoventricular node in control. There are no ventricular extrasystoles. The QRS complex is 0.05 second. The T wave in lead I is small and sharply inverted; elsewhere this wave is erect. The S-T segment in leads II and IV is elevated and is slightly so in lead III. The diagnosis was stretches of bradycardia, with the auriculoventricular node in control, and serious myocardial damage on the basis of coronary blocking but with atypical localization.

ammonium chloride was 50 mg. by vein. The dog showed no ill effects from the drug other than an increase in the heart rate which lasted about fifteen minutes.

Electrocardiograms taken at intervals after coronary ligation revealed no differences between the control group and those treated with tetra-

ethylammonium chloride daily. Figures 7 to 10 are electrocardiographic tracings of animals receiving tetraethylammonium chloride after coronary ligation. When they are compared with figure 6 from a normal dog, it is seen that no outstanding improvement or deterioration can be attributable to the drug.

COMMENT

Tetraethylammonium chloride (etamon®) was found to be effective in preventing weakness and gangrene of the hindlegs of dogs after ligation and the division of the abdominal aorta immediately above its bifurcation.

Perhaps this favorable effect is due to the action of the drug on the collaterals which come off cephalad to the site of division of the aorta. These vessels are quite numerous in the dog, especially the internal mammary-epigastric anastomosis in females. The therapeutic effect of the drug, blocking impulses across the ganglions pertaining to these collaterals, causes vascular dilatation.

No favorable effect was observed when the main stem mesenteric vessels were ligated and the drug administered. When the small vessels of the bowel were ligated, administration of the drug produced an unfavorable effect.

The physiologic responses of the autonomic system to the drug are still not completely understood, and the behavior of the drug itself in the hands of different investigators has not been uniform. Different interpretations have been drawn regarding its role in vascular dilatation and the relief of spasm.

DeBakey, Burch, Ray and Ochsner,[12] using careful plethysmograms and recordings of skin temperature of the extremities, found that very little vasodilatation was produced by one intravenous injection of tetraethylammonium chloride.

Pearl,[13] likewise, found that the rise in skin temperature in fingers and toes (the best indication, according to him, of the release of vascular spasm) of patients with peripheral arterial disease was much less after administration of tetraethylammonium chloride than after nerve block with procaine.

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12. DeBakey, M. E.; Burch, G.; Ray, T., and Ochsner, A.: The "Borrowing-Lending" Hemodynamic Phenomenon and Its Therapeutic Application in Peripheral Vascular Disturbances, Am. J. Surg. **126**:850, 1947.

13. Pearl, F.: Tetraethyl Ammonium Chloride, Its Effect on Surface Temperatures of Extremities in Peripheral Vascular Conditions, Am. J. Surg **128**:1092, 1948; Effects on Surface Temperatures of Arterio-Sclerotic Extremities, ibid. **128**:1100, 1948.

Brown, Allen and McCraig [14] found that the drug would reduce blood pressure of hypertensive patients much more readily after sympathectomy than before the operation. One half to one third the amount was effective after sympathectomy, and the effect lasted longer. The group of patients were of the type in whom sympathectomy does not readily reduce blood pressure to normal, but 200 mg. of the drug produced this effect in most of them. These authors expressed the belief that the drug does not act in a more concentrated manner on the ganglions which remain after sympathectomy, because very large doses before sympathectomy did not reduce the blood pressure of hypertensive patients to normal. They felt, rather, that in some way either the arterioles became more susceptible to the drug or that the remaining ganglions might be more completely blocked after operation than before.

Laufman,[15] by direct microscopy on the small arterioles of the dog, has emphasized the tremendous role which reflex spasm plays when an artery or vein is occluded. Temporarily occluding the mesenteric vein will cause the small arteries to contract to one eighth their normal size, and this residual spasm will remain for a considerable time. He has given the following explanation of our failure to observe any benefit from the drug after mesenteric ligation [16]: Strangulation of a loop of bowel is analogous to a peripheral vascular occlusion. There is stimulation of the afferent sympathetic nerve fibers and ganglions, with resulting reflex vasospasm of the segment of bowel involved. Occlusion and division of a small mesenteric vessel or even handling the mesentery of the bowel produces a similar spasm. When the drug is given to such an animal it apparently dissipates itself by acting on the unstimulated ganglions in the rest of the body, since these are the paths of least resistance. The ganglions harboring the stimulus of the occlusion are thereby left relatively unaffected by the action of the drug. This is especially true if the stimulus is strong. Consequently, the general vasodilatation in other parts of the body results in the removal of blood from the stimulated area. Thus additional local spasm is produced rather than dilatation, and thus a reversal of the effect from the drug is caused.

14. Brown, H. S.; Allen, E. V., and McCraig, W.: The Effect of Tetraethyl-Ammonium Chloride on Blood Pressure Before and After Sympathectomy for Hypertension, Proc. Staff Meet., Mayo Clin. **23**:94, 1948.

15. Laufman, H.; Martin, W. B., and Tuell, S. W.: Rationale of Therapy in Acute Vascular Occlusions Based on Micrometric Observations, Ann. Surg., to be published.

16. Laufman, H.: Personal communications to the authors.

CONCLUSIONS

1. Experimentally, tetraethylammonium chloride (etamon®) is of definite value in preventing ischemic gangrene, muscular weakness and subsequent paralysis produced when the aorta is ligated and divided just above the bifurcation. The use of this drug in certain injuries of peripheral vessels appears to be of value.

2. The action of tetraethylammonium chloride observed on the mesenteric vessels does not appear to be analogous to the action observed in peripheral vessels.

3. Vasospasm is not prevented or abolished by tetraethylammonium chloride when it occurs in the mesenteric vessels or in the intestinal musculature. Further evidence of the inability of the drug to relieve vasospasm is noted by the fall in serosal temperature.

4. Tetraethylammonium chloride is not indicated in mesenteric thrombosis or in mechanical intestinal obstruction as an agent for the relief of vasospasm occurring in these conditions. Likewise, the drug is not advocated as a means of determining the viability of a previously strangulated loop of bowel in which vascular occlusion has occurred.

5. Neither detrimental nor advantageous effects were observed in dogs after experimental ligation of coronary vessels.

EFFECT OF DISTENTION ON INTESTINAL REVASCULARIZATION

RUDOLF J. NOER, M.D.
AND
JOHN WILLIAM DERR, M.D.
DETROIT

DISTENTION of the small intestine has been shown to exert a deleterious effect on the blood flow through the intestinal wall in experimental animals and it is reasonable to expect some degree of correlation between the findings in animals and the situation in man. Indirect evidence that this is true is to be found in gross and microscopic study of material observed in the operating room and at autopsy. Direct observation, however, of the precise effect of varying degrees of distention on the intramural circulation in man during life presents obvious difficulties. It therefore seems worth while to present data based on the use of injection technics in the study of human autopsy material.

Intraluminal pressures in obstructed intestines of dogs have been measured by Owings, McIntosh, Stone and Weinberg [1]; Burget, Martzloff, Suckow and Thornton [2]; Antoncic and Lawson [3]; Sperling, Paine and Wangensteen,[4] and others. These studies were carried out in the living animal intestine. The results are therefore not directly applicable to the present study of excised human intestine, which obviously con-

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This investigation was supported by a research grant from the Division of Research Grants and Fellowships of the National Institute of Health, U. S. Public Health Service.

1. Owings, J. C.; McIntosh, C. A.; Stone, H. B., and Weinberg, J. A.: Intraintestinal Pressure in Obstruction, Arch. Surg. **17**:507 (Sept.) 1928.

2. Burget, G. E.; Martzloff, K.; Suckow, G., and Thornton, R. C. B.: The Closed Intestinal Loop: I. Relation of Intraloop (Jejunum) Pressure to the Clinical Condition of the Animal, Arch. Surg. **21**:829 (Nov.) 1930.

3. Antoncic, R. F., and Lawson, H.: The Muscular Activity of the Small Intestine in the Dog During Acute Obstruction, Ann. Surg. **114**:415, 1941.

4. Sperling, L.; Paine, J. R., and Wangensteen, O. H.: Intra-Enteric Pressure in Experimental and Clinical Intestinal Obstruction, Proc. Soc. Exper. Biol. & Med. **32**:1504, 1935.

siders only the purely mechanical effect of distention on the intramural vessels. Sperling, Paine and Wangensteen [4] also measured the intraenteric pressure in 5 cases of mechanical obstruction of the small bowel at the time of enterostomy by connecting the enterostomy tube to a manometer. Sustained pressures varied between 4 and 18 cm. of water, whereas pressures of 20 to 30 cm. developed during active peristalsis. Reports of accurate determination of intraluminal pressures in distended human intestine in the unopened abdomen without concomitant decompression have not been found. This is obviously a difficult problem but one deserving of further investigations.

Van Zwalenburg [5] (1907) inserted a cannula, carrying a small lamp, into the lumen of the intestine of the dog and studied the effect of intraenteric pressures on the blood flow through the intestinal wall by means of low power microscopy. His report is as follows:

> At 30 mm. mercury pressure we found that some capillary streams were arrested. At 60 mm. many small veins had their currents arrested, and in most of them the stream was so slow that individual corpuscles could be seen. At 90 mm. all blood streams were moving slowly and many were not moving at all. One was impressed with the difficulties encountered by the circulation in its attempt to find some point of least resistance through which the stream might insinuate itself. Currents would at one time go in one direction and the next moment in the opposite. At the point of branching of vessels, streams were seen going in all sorts of directions.
>
> At 130 mm. all circulation had ceased—the corpuscles standing still in the blood vessels. Many vessels, however, still carried the impulse of the heart beat—the corpuscles moving to and fro, but retaining their relative positions in the field. This pulsation was seen in some of the largest and the most superficial arteries after the pressure was carried up to 250 mm.

Gatch, Trusler and Ayres [6] (1927) studied blood flow through the intestinal wall in dogs by collecting all venous return from isolated obstructed loops. The rate of return flow was inversely proportional to the degree of distention. They also noted a constant residual blood flow from anastomotic vessels in the mesentery and along the mesenteric border, however great the distention. Complete anemia was observed on the antemesenteric border of the bowel when the intraenteric pressure equaled the systemic blood pressure. Morton [7] (1929) presented low power photomicrographs of injected duodenum and ileum of the dog with and without distention. The interference with filling of the

5. Van Zwalenburg, C.: Strangulation Resulting from Distention of Hollow Viscera, Ann. Surg. **46**:780, 1907.

6. Gatch, W. D.; Trusler, H. M., and Ayres, K. D.: Effects of Gaseous Distention on Obstructed Bowel, Arch. Surg. **14**:1215 (June) 1927.

7. Morton, J. J.: Differences Between High and Low Intestinal Obstruction in the Dog: Anatomic and Physiologic Explanation, Arch. Surg. **18**:1119 (April) 1929.

finer vessels produced by distention is well shown, although the degree of intraenteric pressure is not stated. Dragstedt, Lang and Millet [8] (1929) reported effects of intraenteric pressures on venous return from the duodenum, jejunum, ileum and colon of the dog and amplified their findings by observations of the transilluminated intestinal wall. Interruption of venous flow occurred at pressures of 35 to 40 mm. of mercury in the jejunum and 55 to 60 mm. in the ileum. Their studies indicated that this obstruction occurred in the wall of the intestine and not in the mesentery. They confirmed the findings of Gatch and his associates [9] as to the residual flow from the mesenteric veins which no amount of intraenteric pressure would abolish. Herrin and Meek [9] reported in 1933 that intraluminal pressures of 50 to 80 mm. of mercury in the dog reproduced the entire clinical picture of intestinal obstruction even though patency of the intestinal lumen was maintained. Gatch and Culbertson [10] (1935) reported that pressures as low as 20 mm. of mercury may produce almost complete ischemia of the intestinal mucosa of the dog. Sperling and Wangensteen [11] (1935) were able to prevent absorption of strychnine from closed ileal loops by intraluminal pressures greater than 100 mm. of mercury and could elicit a strychnine effect only after reduction of pressures below 70 mm. Absorption occurred more readily after damage of the intestinal wall by protracted distention.

Lawson and Chumley [12] (1940) studied differential pressures between systemic vessels and those supplying isolated loops of ileum in dogs. Blood flow was only momentarily interrupted by pressures below 30 mm. of mercury. Higher pressures below mean arterial pressure produced marked initial reduction in flow, followed by partial recovery in a few seconds. Denervation did not alter the results, and they suggest intrinsic nervous mechanisms as the means for compensation. Oppenheimer and Mann [13] (1943), transilluminating the wall of the

8. Dragstedt, C. A.; Lang, J. F., and Millet, R. F.: The Relative Effects of Distention on Different Portions of the Intestine, Arch. Surg. **18**:2257 (June) 1929.

9. Herrin, R. C., and Meek, W. J.: Distention as a Factor in Intestinal Obstruction, Arch. Int. Med. **51**:152 (Jan.) 1933.

10. Gatch, W. D., and Culbertson, C. G.: Circulatory Disturbances Caused by Intestinal Obstruction, Ann. Surg. **102**:619, 1935.

11. Sperling, L. and Wangensteen, O. H.: Transperitoneal Absorption: VI. Significance of Impaired Viability and Influence of Distension on its Occurrence, Proc. Soc. Exper. Biol. & Med. **32**:1385, 1935.

12. Lawson, H., and Chumley, J.: The Effect of Distention on Blood Flow through the Intestine, Am. J. Physiol. **131**:368, 1940.

13. Oppenheimer, M. J., and Mann, F. C.: Intestinal Capillary Circulation During Distention, Surgery **13**:548, 1943.

rat intestine, found no change in the intraparietal capillary circulation at pressures of 10 to 20 mm. of mercury. At 30 to 50 mm. there was increasing interference with capillary circulation, while at 60 mm. "all capillary flow had ceased and only in the largest vessels was blood flowing rapidly. At 70 mm. no flow was seen except in one or two large vessels (arterioles and venules) which had a sluggish, oscillating flow and at 80 mm. even this had stopped."

As stated earlier, direct observation of blood flow through the wall of the living human intestine is difficult to observe, and to our knowledge no correlation of such observations with the degree of intraenteric pressure has been reported. Van Beuren [14] (1929) presented an interesting account of the effect of distention on the vessels of the intestinal wall. His illustrations, concerned chiefly with intestinal perforations following distention, include photomicrographs of dog intestine and human autopsy material. Pressure measurements are not included, but the circulatory effects presumably produced by distention are well demonstrated.

Experimental data from these laboratories [15] indicate that injection studies of excised intestine can be utilized for guarded inferences as to the situation existing in life. Investigation of routes for revascularization following experimental mesenteric occlusion indicated that the maximum degree of devascularization compatible with life of the experimental animal was likewise the maximum area which could be filled through collateral channels by injection technics. Circulatory interruption of sufficient extent to cause death of the animal also resulted in failure to fill similar areas by injection. It thus appears that injection technics may be utilized for investigation of circulatory situations in man which cannot otherwise be attacked with presently available methods.

METHODS

Human autopsy material was utilized for all these studies, the entire small intestine being removed as soon after death as possible, with the blood supply preserved intact. Twenty such specimens, varying between 18 and 20 hours post mortem, were used. Good injections were obtained in all cases, although capillary filling was invariably more nearly complete in the fresher material. Extravasations occurred but rarely and only in the longer dead intestines. Loops chosen for study were all from the lower part of the jejunum or the upper part of the ileum. In every case the entire intestine was injected through the superior mesenteric artery, thus providing normal areas for comparison with the degree of filling obtained in the distended loops.

14. Van Beuren, F. T. Jr.: The Mechanism of Intestinal Perforation Due to Distention, Ann. Surg. **83**:69, 1926.

15. Derr, J. W., and Noer, R. J.: Experimental Mesenteric Vascular Occlusion, Surg., Gynec. & Obst., to be published. Noer, R. J., and Derr, J. W.: Revascularization Following Experimental Mesenteric Vascular Occlusion, Arch. Surg., **58**:576 (May) 1949.

India ink diluted in bovine plasma proved the best medium. There is little diffusion of this material, and viscosity determinations indicate that it closely approximates the viscosity of blood. All injections were made at room temperature, at pressures between 100 and 150 mm. of mercury. Slightly more rapid filling was obtained with the higher pressures, but complete filling was routinely obtained with pressures of 100 mm. of mercury or even lower. Drying of the intestine was avoided by repeated spraying of the surface with an atomizer.

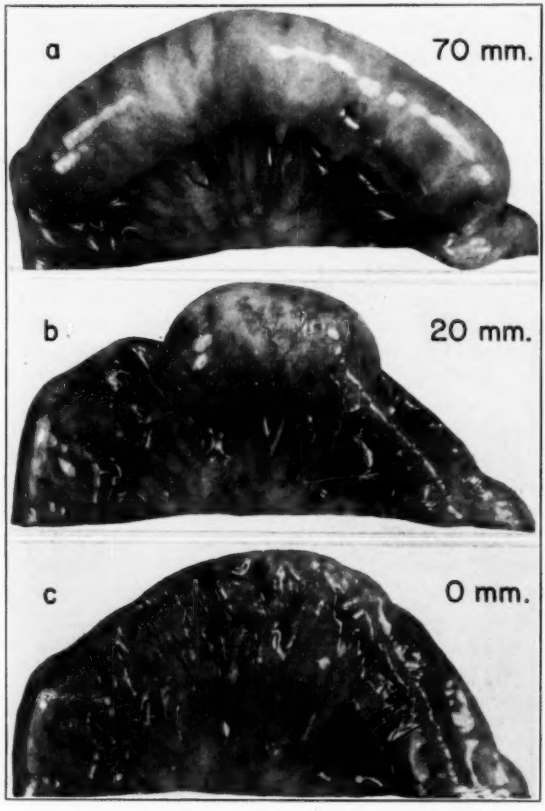

Fig. 1.—Specimens of human intestine injected with india ink after distention. Note absence of filling at pressure of 70 mm. of mercury and filling of the larger arteries at 20 mm. but complete filling only after release of distention. Unfortunately, the contrast between filled and noninjected intestine, seen clearly in color cinephotography, is not adequately reproduced in black and white.

Intraenteric distention was produced by air inflation of a condom balloon introduced into the loop being studied, the pressure measured by a mercury manometer. This may introduce an error in pressure measurement equal to the inherent resistance of the latex balloon. Inflation of this balloon to the size

ordinarily used in the course of the experiments was found to require pressure of not more than 5 mm. of mercury. Actual intraenteric pressures in these experiments may therefore be approximately 5 mm. of mercury less than the recorded pressures which are reported. Injections were started above 70 mm. of mercury (this being the pressure required to prevent filling in most instances), and injecting pressure was constantly maintained throughout the process of gradual deflation of the balloon by steps of 10 mm. each.

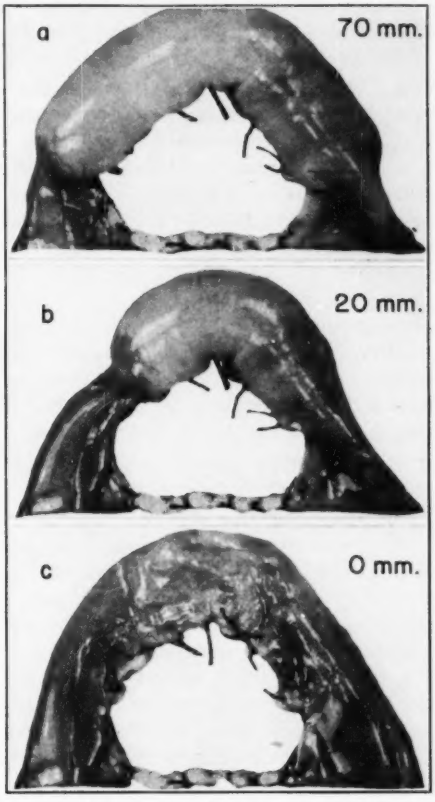

Fig. 2.—Specimens of human intestine injected with india ink after division of the vasa recta followed by distention. Note that no filling of the loop occurs while distention remains but that good vascular filling is obtained after deflation (compare with figure 1).

Results were recorded for repeated study by slow motion cinephotography (films taken at 32 frames per second were projected for study at 16 frames per second, thus reducing the apparent speed of injection by approximately one half).

Some of the specimens were preserved by fixation in formaldehyde solution U.S.P. and cleared by a previously described modification of the Spalteholz technic.[16]

RESULTS

Intraenteric pressures of 70 mm. of mercury or higher prevent filling of the distended area of the intestine, even when all the mesenteric vessels remain intact. Gradual deflation reveals that the larger arteries begin to fill at 60 to 50 mm., and that they are fairly well injected at pressures of 20 to 30 mm. Complete capillary filling, however, does not occur until complete deflation has been produced (fig. 1).

Ligation of the vasa recta supplying the distended loop greatly accentuates the interference with filling produced by distention, since all filling must then take place by means of anastomoses within the intestinal wall. In these circumstances the distended loop fills only from its extremities as the balloon is deflating in these areas; the central portion of the loop remains uninjected until complete deflation of the balloon has been accomplished (fig. 2).

COMMENT

It should be recognized at the outset that the situation which exists in the excised, nonviable intestine is vastly different from that which exists in life. Such factors as vasodilation and vasoconstriction, contractility of muscle and variations in tissue tension must all be of great importance in determining the reaction of the intestine and its circulation to varying degrees of distention. However, these very factors tend to complicate the entire picture and make interpretation of their individual importance a matter of considerable difficulty.

The studies here reported represent a simple and direct approach to the purely mechanical effect of distention on the vessels lying within the wall of the intestine. The results, for the most part, are in accord with opinions expressed by many investigators, and they differ but little from what might be predicted on the basis of various animal experiments. However, it appeared worth while to present the findings for reemphasis of the fact that distention, even in minor degrees, results in definite and often serious interference with the circulation within the intestinal wall. Whether the various physiologic factors mentioned increase or decrease this circulatory embarrassment, we are not prepared to say. Certain it is, however, that the purely mechanical effect of distention as herein demonstrated presents a serious hazard to the patient with intestinal distention, whatever the cause. The urgent need for prompt and complete decompression of the intestine is obvious.

16. Noer, R. J.: The Blood Vessels of the Jejunum and Ileum: A Comparative Study of Man and Certain Laboratory Animals, Am. J. Anat. **73**:293, 1943. Lathrop, G. E., and Krupp, R.: Microscopy of Latex Rubber-Injected Specimens, Am. J. Clin. Path. **14**:128, 1944.

CONCLUSIONS

Injection studies of the effect of distention on the intramural vessels of excised human small intestine reveal the following facts:

1. Intraenteric pressures above 70 mm. of mercury prevent filling of all vessels within the wall.

2. When the vasa recta and arcuate vessels remain intact, the larger arteries will fill despite intraluminal pressures of 20 to 40 mm. of mercury.

3. Complete capillary filling can be obtained only when the intraenteric pressure is less than 10 mm. of mercury.

4. Interruption of the vasa recta supplying a distended loop results in inability completely to inject this partially devascularized loop until distention has been eliminated.

OBSERVATIONS IN STRANGULATION OBSTRUCTION

II. The Fate of Sterile Devascularized Intestine in the Peritoneal Cavity

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IN EACH of the several extensive reviews on the subject of intestinal strangulation obstruction,[1] certain questions concerning the nature of toxicity have been left open for speculation. With the advent of such therapeutic advances as replacement of fluids and electrolytes, broader use of blood transfusion, antibiotic therapy and intubation, great strides have been made toward lowering the basic mortality as well as the operative mortality. These advances, great as they are in the therapeutic sense, served in recent years to cool experimental interest in the nature of the toxicity in this affliction. However, during World War II much work was done along parallel lines on the general problem of tissue autolysis in shock, and a large part of the work is directly applicable to the problem of strangulation. Chemotherapy and antibiotic therapy have opened new avenues both in experimental investigation and in clinical practice, since the control of the bacterial factor of the toxicity has resulted in a remarkable diminution of the ill effects from loop strangulations.

The extensive experimental background is well known to those interested in the pathologic physiology of intestinal obstruction, but

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From the Departments of Surgery and Bacteriology, Northwestern University Medical School.

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1. (*a*) Aird, I.: Morbid Influences in Intestinal Obstruction and Strangulation, Ann. Surg. **114**:385, 1941. (*b*) Besser, E. L.: Cause of Death in Cases of Mechanical Intestinal Obstruction, Arch. Surg. **41**:970 (Oct.) 1940. (*c*) Cooper, H. S. F.: The Cause of Death in High Obstruction in Dog: Anatomic and Physiologic Explanation, ibid. **17**:919 (Dec.) 1928. (*d*) Morton, J. J.: Differences Between High and Low Intestinal Obstruction, ibid. **18**:1119 (April) 1929.

it might be advisable to review briefly a few of the crucial experiments in this field.

It has been known for many years from the work of Stone, Bernheim and Whipple [2] that neither frank septicemia nor the loss of fluids and electrolytes from vomiting could explain death from intestinal obstruction. Since these investigators introduced the technic of the isolated loop experiment, which did away with the factor of obstruction, much work has been done by the use of this technic to demonstrate the effects of strangulation. Davis and Stone [3] and Murphy and Brooks [4] were among the investigators who believed that toxins arose from such a loop. Dragstedt,[5] in similar experiments, washed the loops out with ether and found that this diminished the toxicity.

Strangulation experiments of many types have been performed. It has been shown repeatedly that if a loop of intestine of medium length is strangulated within a sterile bag to prevent peritoneal absorption, death is delayed indefinitely provided the lumen is reconstituted. In the absence of the bag, death occurs within two to five days, not necessarily from peritonitis and without septicemia.[6]

Much subsequent work was devoted to the question of the similarity of the toxic picture in strangulation to that of shock. Indeed, fresh postmortem studies showed "wet" organs, indicating a generalized state of increased capillary permeability.[7] Many searches have been made for substances which might produce this state. Among some of the substances which have been implicated are histamine,[6] H substance,[8] adenosine triphosphate [9] and leukotaxine,[10] as well as others. That one

2. Stone, H. B.: Bernheim, B. M., and Whipple, G. H.: Intestinal Obstruction: A Study of the Toxic Factors, Bull. Johns Hopkins Hosp. **23**:159, 1912.

3. Davis, D. M., and Stone, H. B.: Studies on the Development of Toxicity in Intestinal Secretion, J. Exper. Med. **26**:687, 1917.

4. Murphy, F. T., and Brooks, B.: Intestinal Obstruction: An Experimental Study of the Causes of Symptoms and Death, Arch. Int. Med. **15**:392 (March) 1915.

5. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: Intestinal Obstruction: II. A Study of the Factors Involved in the Production and Absorption of Toxic Materials from the Intestine, J. Exper. Med. **30**:109, 1919.

6. Aird, I., and Henderson, W. K.: Intestinal Strangulation: The Histamine Content of the Peritoneal Transudate from Strangulated Intestinal Loops, Brit. J. Surg. **24**:777 (April) 1937.

7. Moon, V. H.: Shock and Related Capillary Phenomena, New York, Oxford University Press, 1938.

8. Dale, H. H.: Conditions Which are Conducive to Production of Shock by Histamine, Brit. J. Exper. Path. **1**:103, 1920.

9. Bielschowsky, M., and Green, H. M.: Shock Producing Factor(s) from Striated Muscle: II. Fractionation, Chemical Properties and Effective Doses. Lancet **3**:153, 1943.

(Footnote continued on next page)

or all of these substances are produced and absorbed by way of the peritoneal surface cannot be denied; yet their mode of production has not been altogether clarified. A further complication in the assumption that these substances are toxic is the fact that subsequent injections of these substances into healthy animals do not always produce the physiologic state seen in the animal with a strangulated loop, even when the factor of obstruction is accounted for. It is possible, therefore, that these substances are merely a reflection of the primary morbid changes, rather than the cause of the toxicity itself.

In the first article of the present series, Laufman and Freed [10] demonstrated the presence of a substance resembling leukotaxine in the transudate from strangulated loops. This substance invariably produced increased capillary permeability and could be neutralized to a certain degree by adrenal cortex extract. The substance was less potent when filtered free of bacteria but still gave a positive reaction to the Menkin test [11] for the production of increased capillary permeability. This led to an attractive theory that, since local fluid loss from the involved loop was insufficient to account for death, a leukotaxine-like substance might produce a state of local and generalized increased capillary permeability and even a state of shock and might account for the tremendous loss of fluid accompanying strangulation obstruction [12] as well as the "wet" organs [7] usually found post mortem. The concomitant work of Abraham and associates at Oxford [13] tended to support this theory. These workers found that large doses of sterile peptic digests contain permeability-increasing polypeptides which, however, only occasionally caused death, although hemocencentration was usually present. Autolytic products alone, while producing local loss of fluid in the peritoneal cavity, did not usually produce general effects after absorption which led to a shocklike state. The investigators concluded, however, that the presence of large masses of autolyzing tissue, such as muscle, must liberate substances of a polypeptide nature which affect profoundly the local blood vessels, causing increased capillary permeability and hence the escape of plasma, thus contributing to the state of shock.

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10. Laufman, H., and Freed, S. C.: Observations in Intestinal Strangulation: I. The Effect of Adrenal Cortical Extract on Its Toxicity, Surg. Gynec. & Obst. **77**:605, 1943.

11. Menkin, V.: Effect of Leukotaxine on Cellular Permeability and on Cleavage Development, Proc. Soc. Exper. Biol. & Med. **44**:588, 1940.

12. Fine, J.; Fuchs, F., and Gendel, S.: Changes in Plasma Volume Due to Decompression of Distended Small Intestine, Arch. Surg. **40**:710 (April) 1940.

13. Abraham, E. P.; Brown, G. M.; Chain, E.; Florey, H. W.; Gardner, A. D., and Sanders, A. G.: Tissue Autolysis and Shock, Quart. J. Exper. Physiol. **30**:79 1940; **31**:41, 1942.

For our present purpose, the question arose as to whether autolysis of devascularized intestinal tissue contributes to the state of toxicity over and above the contribution by the bacteria. The present report deals with the effects of autolysis of intestinal tissue in the peritoneal cavity in the relative absence of bacteria.

Various types of dead tissue have been placed into the peritoneal cavities of experimental animals by other investigators. Andrews and associates [14] placed a detached piece of liver in the free peritoneal cavity and found it to cause death. Ellis and Dragstedt [15] did liver implantation experiments and regarded the lethal outcome the result of bacterial toxemia rather than toxemia due to absorption of autolytic products. They indicated that organisms are apparently normal saprophytes of tissue and hence most workers had been quite unable to obtain adult tissues free from bacteria. When they implanted fetal livers obtained by cesarean section, eventual absorption took place without evidence of toxicity.

Mason and Richardson,[15a] using blood pressure as an index of shock following the intravenous injection of filtrates of peripheral muscle, have shown that when the action of bacteria was prevented during autolysis the injection of the resulting filtrates produced no appreciable effect. When bacteria were allowed to grow during autolysis, the filtrate caused a marked drop in blood pressure followed by a rise. Green and Bielschowsky [16] planted striated leg muscle into the peritoneal cavities of animals without antibacterial protection. The toxic effects thus produced were assumed to stem from proteolysis alone. Chemical analysis indicated that adenosine triphosphate was the responsibile agent. It has been shown that less than 5 Gm. per kilogram of wet muscle tissue causes no ill effect but more than this amount causes toxicity and death when placed in the peritoneal cavity. This was true whether the muscle was extracted and powdered [17] or used in its fresh state. These experiments, too, were done before the advent of antibiotic drugs. Yet Parsons and Phemister in 1930 [18] implanted the

14. Andrews, E.; Rewbridge, A. G., and Hrdina, L.: Causation of Bacillus Welchii Infections in Dogs by Injection of Sterile Liver Extracts, Surg., Gynec. & Obst. **53**:176, 1931.

15. Ellis, J. C., and Dragstedt, L. R.: Liver Autolysis in Vivo, Arch. Surg. **20**:8 (Jan.) 1930.

15a. Mason, E. C., and Richardson, D. L.: Traumatized Muscle Tissue as a Factor in the Production of Shock, Surg., Gynec. & Obst. **85**:71, 1947.

16. Green, H. N.: Shock-Producing Factor(s) from Striated Muscle: I. Isolation and Biological Properties, Lancet **2**:147, 1943. Bielschowsky and Green.[9]

17. Muirhead, E. E., and Hill, J. M.: Shock Resulting from the Implantation Intraperitoneally of Reconstituted Desiccated Muscle, J. Lab. & Clin. Med. **29**:337, 1944.

18. Parsons, E., and Phemister, D. B.: Hemorrhage and "Shock" in Traumatized Limbs: Experimental Study, Surg., Gynec. & Obst. **51**:196, 1930.

rectus abdominis muscle into the peritoneal cavities of 2 dogs without producing toxic symptoms. Laufman and Method [19] recently implanted 6 Gm. per kilogram of leg muscle into the peritoneal cavities of dogs protected with adequate doses of penicillin. The animals showed no ill effects, and several weeks later almost no trace of the previously implanted muscle could be found. Aird [18] placed strips of embryo guinea pig intestine into the peritoneal cavities of cats. Such strips were sterile and caused no deleterious effects, dissolving after several weeks. When bacteria were introduced together with the embryo intestine, the host animals died.

This brief perusal of the pertinent literature indicates that sterile tissue placed in the peritoneal cavity will undergo autolysis without producing either a shocklike state or death. If this is so, we thought that

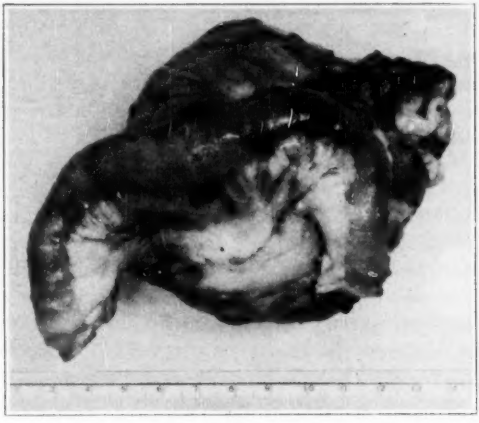

Fig. 1.—Appearance of cystlike dilatation of isolated loop shown attached to adherent normal intestine (in front). This occurred in an occasional animal when open ends of isolated loop closed spontaneously, allowing gradual distention of loop (see text).

it should be possible to determine whether in strangulation of the intestine the toxic effects are due mainly to the bacteria in the involved lumen or whether autolysis of the devascularized bowel is the main source of toxic substances. We therefore set out to determine the effect of "sterile" autolysis of the host's own intestinal tissue in the peritoneal cavity, using dogs.

Our first 17 dogs were prepared with the standard type of isolated loop of ileum as devised by Stone, Bernheim and Whipple.[2] The segment was washed out with saline solution and the ends allowed to

19. Laufman, H., and Method H.: Unpublished data.

remain open, essentially as Dragstedt, Moorhead and Burcky [20] had done. We found that with a successful anastomosis such animals would survive with no ill effects and the ends of the segment would gradually close over a period of four to six weeks. However, at the second operation, cultures taken from the center of such a loop invariably revealed a luxurious growth of mixed bacteria. Hence, with this method we were not able to produce "sterile" loops. Even when such animals were placed on a penicillin regimen, the loop yielded the same type of growth but in lesser amounts. An interesting feature of such animals was that the loop did not become distended, since the mucosal secretions drained freely into the peritoneal cavity until the time of spontaneous closure.

Occasionally, such a loop, some time after closure (four to six weeks after operation) would suddenly distend and even rupture, causing

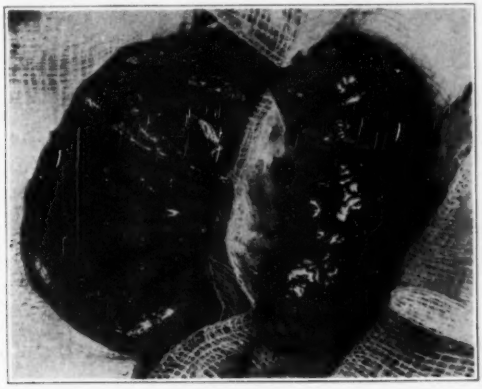

Fig. 2.—Appearance of amputated loop which had become wrapped in omentum and had become revascularized (right). Normal bowel shown on left. This was prevented by amputation of omentum in later experiments (see text).

death of the animal from peritonitis. In a few instances, this distention was so gradual that the blood supply was not endangered and a cyst-like structure resulted (fig. 1). Although the organisms within such a loop or cyst were undoubtedly of low virulence, they were nonetheless present. The presence of bacteria became all the more evident by the sudden death of a few animals as late as five weeks following obstruction of the loop. In such animals autopsy showed distention and necrosis of the loop and peritonitis. It appeared that when there was dead or dying tissue on which to grow, the bacteria became pathogenic once

20. Dragstedt, L. R.; Moorhead, J. J., and Burcky, F. W.: Intestinal Obstruction: An Experimental Study of the Intoxication in Closed Intestinal Loops, J. Exper. Med. **25**:421, 1917.

more. Our failure to produce sterile loops in which the bacteria would be incapable of returning to a state of virulence, therefore, caused us to alter our technic.

Another feature of these preliminary experiments was the striking observation that whenever the blood supply to one of these closed loops was severed and the loop placed back into the peritoneal cavity, it soon acquired a new blood supply through omental and serosal adhesions (fig. 2). This was especially true if the animal was protected with penicillin for the first few days postoperatively. The experiments of Sarnoff and Poth [21] in which a large segment of small intestine was deprived of its venous drainage after "sterilization" of the intestine

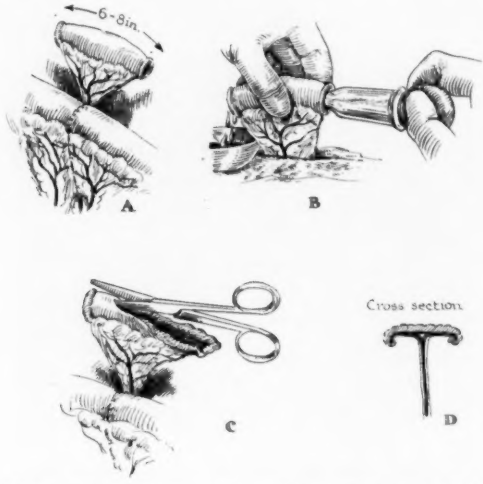

Fig. 3.—Technic of preparing open isolated intestinal loop (initial operation). *A*, segment of ileum removed from continuity allowing mesentery to remain intact; continuity of bowel reestablished by anastomosis. *B*, loop washed with sterile saline solution until washings are clear. *C*, segment cut open in its entire length. *D*, cross sectional appearance of open bowel with mesenteric attachment. At the second operation, several weeks later, the mesenteric pedicle is cut and the omentum is amputated.

with succinylsulfathiazole (sulfasuxidine®) indicated that such segments would survive in most instances when the bacterial count was low. More recently, Davis and associates [22] obtained similar results with

21. Sarnoff, S. J., and Poth, E. J.: Intestinal Obstruction: I. The Protective Action of Succinylsulfathiazole Following Simple Venous Occlusion, Surgery **16**:927, 1944.

22. Davis, H. A.; Gaster, J.; Marsh, R. L., and Pritel, P. A.: The Effect of Streptomycin in Experimental Strangulation of the Bowel, Surg., Gynec. & Obst. **87**:63, 1948.

streptomycin. Apparently, in each instance a new blood supply was formed from omental and serosal adhesions as well as from revascularization from the mesentery. The bowel in these experiments apparently never reached the stage of irreversible autolysis but, being almost sterile, was able to survive until a new blood supply was formed. These experiments, therefore, although indeed remarkable, did not demonstrate the effect of dead sterile intestinal tissue on the animal but did emphasize the importance of bacteria in such lesions.

Harper and Blain [23] placed penicillin into isolated closed loops and found that it protected the animal and prolonged life. Later, Blain [24] used penicillin in strangulated low ileal obstruction, together with whole

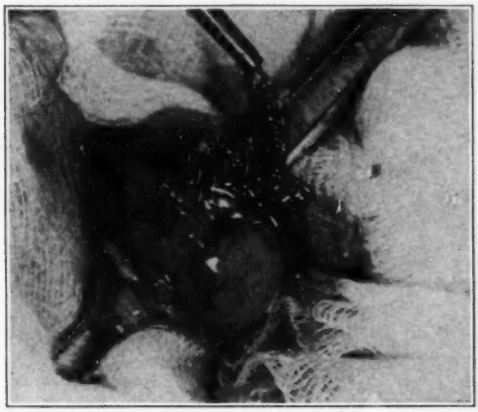

Fig. 4.—Appearance of devascularized intestine three weeks after second operation. Note gelatinous appearance of partially autolysed tissue.

blood and isotonic sodium chloride solution, to combat shock, hemorrhage and loss of chloride and water. He found that such animals lived considerably longer than did the similarly treated controls without penicillin and that resection could be delayed with successful results.

There seems to be little question that bacteria are important in the toxic features of strangulation obstruction, but the isolated effects of sterile autolysis of dead intestinal tissue have apparently not been adequately demonstrated.

23. Harper, W. H., and Blain, A.: The Effect of Penicillin in Experimental Intestinal Obstruction, Bull. Johns Hopkins Hosp. **76**:221, 1945.

24. Blain, A.: Penicillin in Experimental Intestinal Obstruction, Surg., Gynec. & Obst. **84**:753, 1947.

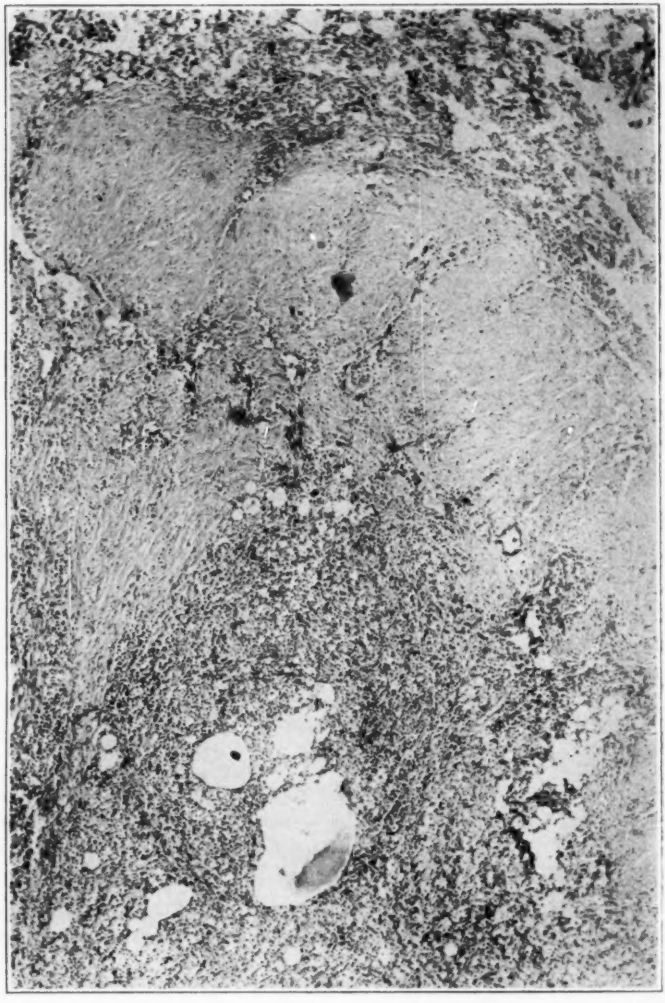

Fig. 5.—Microscopic appearance of devascularized intestine shown in figure 4. There is intense polymorphonuclear infiltration of all layers, and the muscularis shows early degenerative changes.

TECHNIC AND RESULTS

In order to satisfy the requirements of an experiment which would obviate the criticism of previous work done in this field, the following were our aims: (*a*) to isolate a segment of appreciable length of the dog's own intestine; (*b*) to devise a means whereby such a segment would become free of pathogenic organisms; (*c*) to sever the blood supply to the segment, and (*d*) to allow the segment to remain in the host's own peritoneal cavity without acquiring a new blood supply, yet permitting peritoneal absorption of any toxic substances which might result.

In 21 dogs a 6 to 8 inch (15 to 20 cm.) loop of the lower part of the ileum was isolated from its continuity and anastomosis created around it. Its blood supply for the present was left intact. The loop was washed out with sterile isotonic sodium chloride solution and cut open in its entire length on the antimesenteric border (fig. 3). The abdomen was then closed. Fourteen animals survived with no apparent ill effects. Of the 7 deaths, 3 were the result of a leaky anastomosis with peritonitis, while 4 resulted from torsion of the mesenteric pedicle with strangulation of the isolated strip. The latter group will be discussed later.

Fig. 6.—Appearance of devascularized intestine six weeks after second operation. The noodle-like remnant is partially adherent to a normal loop of intestine.

At the second operation, performed on the 14 surviving animals six to eight weeks later, many adhesions were found about the segment and there was considerable mucus entrapped in these adhesions. In several of the animals the exudate was caseous in character. At this operation the segment was cut free of its mesenteric blood supply and of all adhesions and literally lifted free from the animal. The omentum was then amputated so that it could not give the segment a new blood

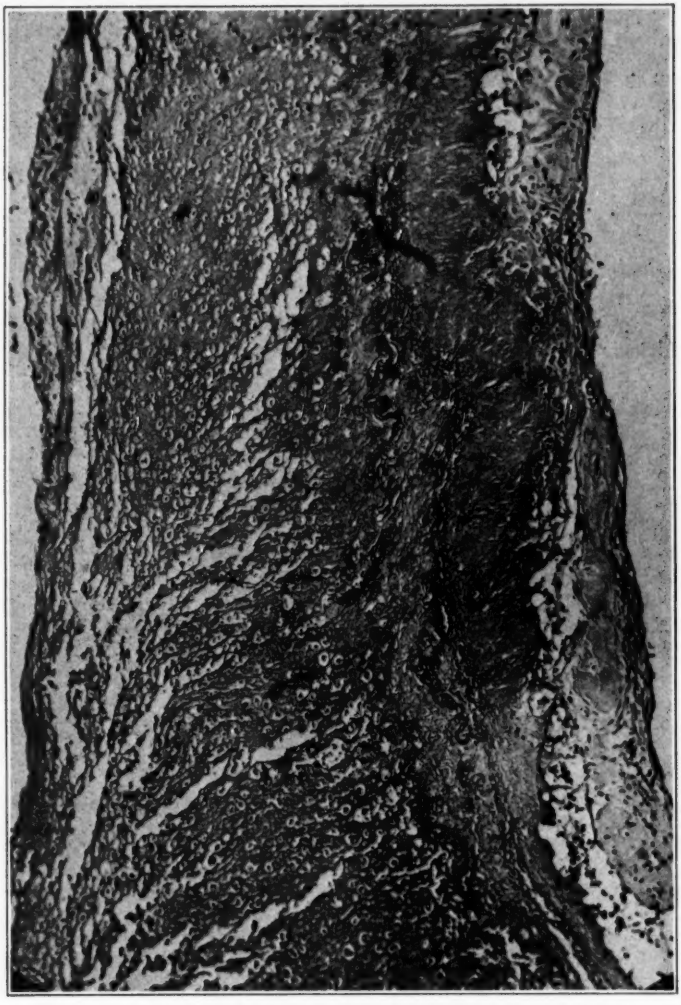

Fig. 7.—Microscopic appearance of devascularized intestine shown in figure 6. Note almost complete degeneration of mucosa. Nuclei in muscularis are pyknotic and surrounded by vacuoles. Muscle fibers in some areas are no longer discernible, leaving only ghost structures.

Organisms Obtained from Tissue Cultures

Dog No.	Culture Taken from Tissue at Second Operation (Blood Supply Intact) Six to Eight Weeks After First Operation	Culture Taken from Tissue at Third Operation (Blood Supply Severed) Three to Fourteen Weeks After Second Operation
19	B. tritus	.....
25	Erysipelothrix (species undetermined)	.....
26	B. subtilis	No growth
27	No growth	No growth
28	No growth	No growth
29	No growth	B. aerogenes
30	Strep. faecalis	.....
31	E. coli Strep. viridans Staph. albus	E. coli
33	E. coli Actinomycetes (species undetermined)	E. coli
35	Strep. faecalis E. coli	No growth
37	E. coli Staph. albus	Staph. albus

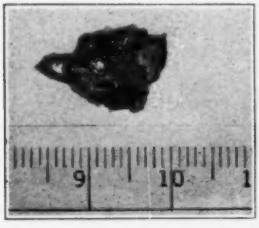

Fig. 8.—Appearance of devascularized intestine eight weeks after second operation. This pea-sized nodule was removed from its attachment to the parietal peritoneum for purposes of photography. Rim of peritoneum can be seen surrounding specimen.

supply by enveloping the segment after it was replaced. Cultures taken from the tissue in 11 different animals at this time (the table) revealed various bacterial forms in 8. These forms were among those commonly found in the intestinal contents. In ordinary circumstances they can assume a pathogenic role only when introduced into the peritoneum from the lumen or when they can propagate on a substratum of dead tissue. In 3 instances there was no growth of bacteria on the culture mediums. We considered such a piece of tissue as "bacteria-free" as it was possible to get in the dog with use of ordinary aseptic surgical technic.

The strip of intestinal tissue was then reimplanted into an adhesion-free portion of the peritoneal cavity, and the abdomen was closed. All but 2 of these animals were treated with penicillin for three days

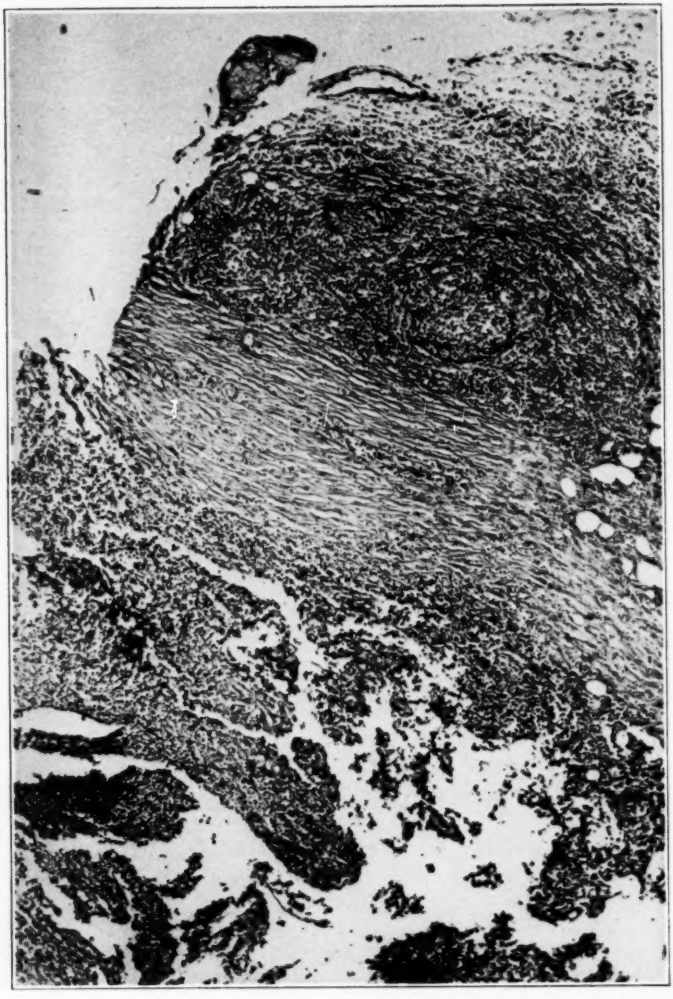

Fig. 9.—Microscopic appearance of devascularized intestine shown in figure 8. Changes are essentially those described in figure 7.

in an attempt to counteract any pathogenic bacteria which may have been present or introduced by the surgical procedures. In the 2 instances in which penicillin was not employed (dogs 27 and 28) the cultures revealed no bacterial growth. After the second operation the animals were watched for periods up to three months. In no instance did any of them show gross signs of distress. On the contrary, many gained weight and all appeared perfectly healthy.

The third operation was then done to expose and examine the area in which the segment was placed (usually the right upper posterior portion of the peritoneal cavity). Cultures taken at this time from 8 animals (the table) revealed no growth in 4 of them. In the remaining 4, the organisms found were Escherichia coli in 2 instances, Staphylococcus albus and Aerobacter aerogenes.

This operation was performed from three to fourteen weeks after the previous laparotomy. At three weeks the tissue presented a gelatinous appearance (fig. 4). At six to eight weeks (in other animals) the tissue no longer bore any gross resemblance to intestinal tissue. In some cases there remained only a thin white strand, similar in appearance to that of a cooked noodle (fig. 6). In other instances the implanted tissue appeared as a small plaque, no larger than a pea, partially adherent to a loop of small intestine or parietal peritoneum (fig. 8). At ten to fourteen weeks (in other animals) only tiny bits of tissue remained, and in 1 animal an exhaustive postmortem search revealed no trace of the tissue except for an almost insignificant adhesion at the site at which it was thought the tissue had been implanted.

COMMENT

These results give us the impression that we have demonstrated that the intraperitoneal autolysis of the host's own intestine in the relative absence of pathogenic bacteria produces no observable deleterious effect on the animal. The technic of graded operations resulted in a progressive diminution in bacterial forms. After the first operation, in which the blood supply was left intact and a large portion of the bacteria were removed by the washing technic, the natural defense mechanisms were able to protect against the invasion by opportunists. At this stage the integrity of the blood supply appeared to be the crucial issue, since when it became endangered by torsion of the mesenteric pedicle the otherwise harmless bacteria were able to propagate on the substrate of dead or dying tissue and cause death.

By the time the second operation was done, the tissue was either free of bacteria or contained only a few remaining bacterial forms. Deliberate severance of the blood supply at this time therefore caused no ill effects, especially since added protection against the remaining opportunists was afforded by a three day course of penicillin.

If it may be inferred that the autolysis of sterile dead tissue in vivo is nontoxic, the natural conclusion would be, therefore, that the toxicity is due entirely to bacteria. On the other hand, the picture is not one of septicemia, as evidenced by our preliminary work and that of others on the nature of the pathologic physiology. Whether the toxicity of autolysis in the presence of bacteria arises from the action of bacteria, bacterial endotoxins, bacterial exotoxins or other spreading factors in the presence of dead tissue cannot be stated with finality at this time, especially since it has been shown recently that penicillin and its impurities offer protection against certain bacterial endotoxins.[25] In the 2 cases in which we did not use penicillin there was no growth on culture, and therefore these cases offer no further information.

We conceive that when the bacteria have a substratum of dead or dying tissue on which to act the combination results in the release of spreading factors which contributes to a state of local and generalized increased capillary permeability, thus contributing to the toxic state. Further, we believe that the release of polypeptides from tissue autolysis is of no consequence unless bacteria are present in sufficient concentration or virulence. If these premises are allowed, it would appear that the toxicity of tissue autolysis is enhanced by the local invasion of bacteria and that the toxicity of the local invasion of bacteria is enhanced by tissue autolysis. Thus the integrity of blood supply is just as crucial as is the bacterial incubation, despite the fact that sterile tissue autolysis is innocuous. Our impressions tend to conform with those originally set forth by Dragstedt.[5]

At the present time we are conducting experiments in this laboratory with the hope of further clarifying the spreading factors. This problem is being approached from the standpoint of enzyme chemistry.

SUMMARY

We have devised a means of demonstrating the effects of autolysis of devascularized intestine in the host's peritoneal cavity in the relative absence of pathogenic bacteria. Our observations indicate that a strip of devascularized ileum will undergo almost complete autolysis in the peritoneal cavity of the dog with no ill effects on the animal provided the tissue is relatively bacteria free. We feel that the implication of this finding is of some importance in the search for toxic factors in intestinal strangulation and allied conditions.

25. Miller, C. P.; Hawk, W. D., and Anderson, W. H.: Protection Against Bacterial Endotoxins by Penicillin and Its Impurities, read before Society of Illinois Bacteriologists, Peoria, Ill., Oct. 15, 1948.

USE OF AN ABDOMINAL FLAP GRAFT IN CONSTRUCTION OF A PERMANENT ILEOSTOMY

CLARENCE W. MONROE, M.D.
AND
JOHN H. OLWIN, M.D.
CHICAGO

THE PATIENT who must have a permanent ileostomy has been materially benefited by the technic of Dragstedt and his associates,[1] who covered the terminal ileum with a split thickness of skin, thus providing a greater length of bowel externally and facilitating the collection of fecal material into a suitable container.

The inherent tendency, however, of both the bowel and a split thickness graft to contract may, over a period of time, result in a marked shortening of the ileostomy. In 1 patient for whom we made such an ileostomy, the original 3½ inches (9 cm.) of skin-covered ileum over a period of eighteen months contracted to the point that only ¼ inch (0.6 cm.) of skin remained and the mucosal edges of the bowel were in contact with the skin of the abdomen. This occurred in spite of a primary take of the graft. There would undoubtedly be less contraction with a thicker graft.

It occurred to us that if one were to utilize a full thickness flap graft containing fat, fascia and its own blood supply the resistance of the skin bordering the ileostomy stoma would be much greater and the possibility of later contraction practically eliminated.

When a patient with familial polyposis involving the entire colon presented himself, the following technic was carried out.

OPERATIVE PROCEDURE

Through a right upper paramedian incision, the terminal 6 inches (15 cm.) of ileum, the right colon and half to two thirds of the transverse colon were resected. The distal 5 inches (13 cm.) of remaining ileum, the opening of which had been closed with a purse string, were then mobilized by severing the vessels just below the distal arches. The viability of the bowel remained intact. A flap of skin was next outlined and elevated (fig. 1) in the right lower abdominal quadrant, the base

From the Department of Surgery, Veterans Administration Hospital, Hines, Ill., and the Presbyterian Hospital, Chicago.

1. Dragstedt, L. R.; Dock, G. M., and Korsner, J. B.: Chronic Ulcerative Colitis: A Summary of Evidence Implicating Bacterium Necrophorum as an Etiologic Agent, Ann. Surg. **114**:653-662, 1941.

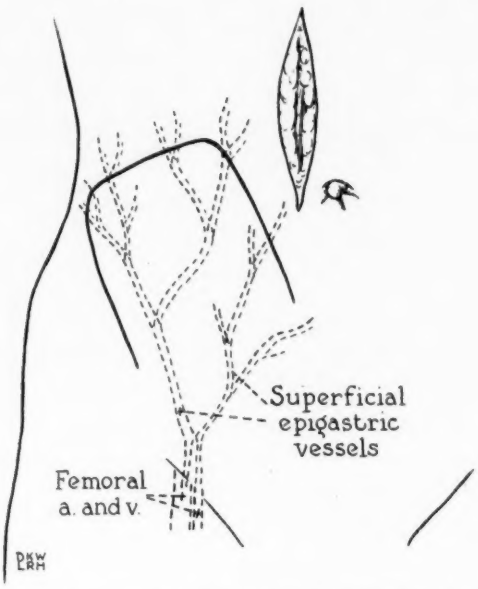

Fig. 1.—Outline of flap on the abdomen, showing distribution of principal blood vessels.

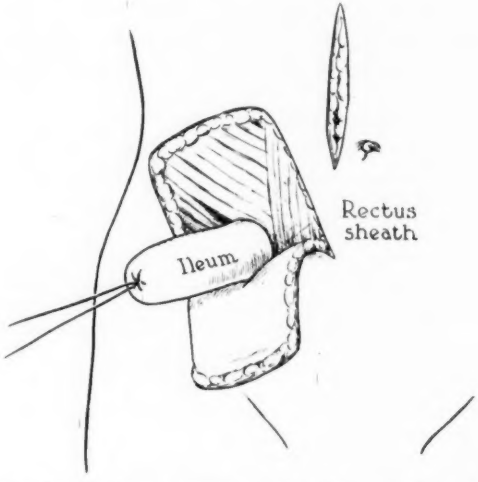

Fig. 2.—The flap has been elevated and the distal end of the ileum brought through a muscle-splitting incision just above the base of the flap.

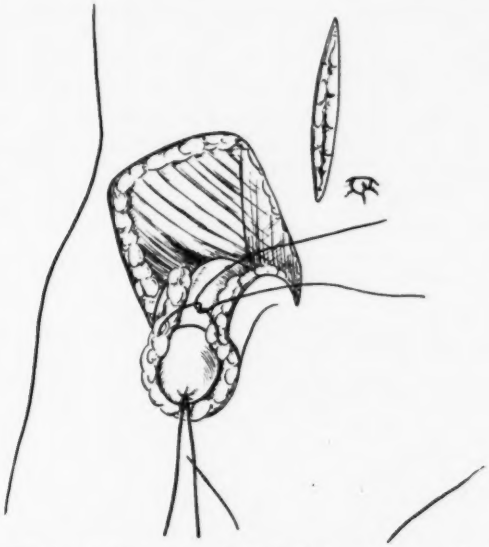

Fig. 3.—The flap is being wrapped about the bowel, and the fascia is closed to itself by suture.

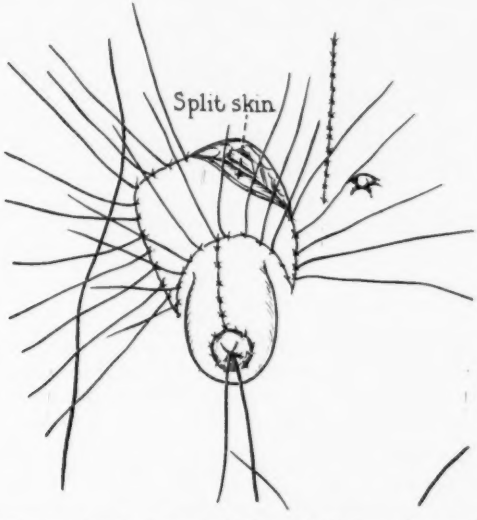

Fig. 4.—The flap has been wrapped about the ileum and sutured to itself on the dorsal aspect. The serosa of the bowel has been sutured to the skin of the flap at its distal open end. The donor site of the flap is covered with a split thickness skin graft.

being directed downward. The flap was approximately 4 inches (10 cm.) in length, 3½ inches (9 cm.) wide and consisted of skin, subcutaneous tissue and fascia with the vessels contained therein. When completely lifted, it appeared to have an adequate blood supply. A muscle-splitting incision was then made through the abdominal wall (fig. 2) just above the central portion of the base of the flap and the ileum brought through this wound. The skin flap was then wrapped about the ileum (fig. 3) and the skin edges approximated, interrupted sutures of fine surgical gut being used in the subcutaneous tissue and nylon sutures in the skin. The mesenteric border of the ileum lay parallel to this suture line. The ileostomy was not opened, and its serosa was sutured directly to the skin edges about the distal end of the newly constructed tube.

The donor site of the flap on the lower right side of the abdomen (fig. 4) was covered with a split thickness skin graft from the anterior aspect of the right thigh.

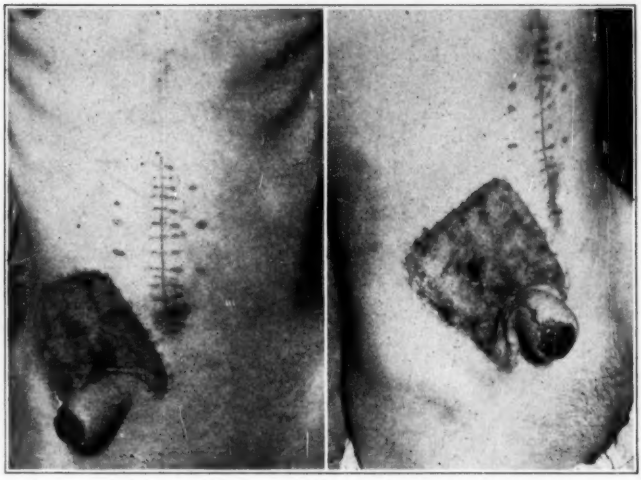

Fig. 5.—Appearance on the eleventh day after ileostomy. The major portion of the split thickness graft in the donor site of the flap has taken well. It is to be noted that a small slough of the margin of the ileum has not yet completely separated to leave a skin-mucosa junction.

This graft was immobilized by tying the sutures, which were left long, over a stent of nylon fabric and moist cotton. The newly made ileostomy was a penile-like structure standing on the abdominal wall about 2½ inches (6 cm.) high. The paramedian incision was then closed and the entire abdomen dressed with a soft bulky pressure dressing which was adequately built up about the ileum and its skin cover to prevent undue pressure.

The ileostomy was not opened at this time but was covered with sufficient dressings generously spread with zinc oxide ointment to protect against spontaneous opening and consequent contamination of the split thickness skin graft. Prior to the operation a Harris tube had been passed well into the lower part of the ileum. The patient was allowed to take water by mouth, and his nutrition was maintained by intravenous administration of fluids. The ileostomy remained closed for seven days following the operation.

The dressing was removed from the split skin graft on the eighth postoperative day, and it was found to have taken almost completely. Subsequently, three or four small areas within the graft broke down (fig. 5), but these healed promptly and the wound has remained clean. There was, naturally, some sloughing of the wall of the ileum at the point where it was sutured to the skin of the flap. When this excess mucosa and bowel wall had sloughed, the skin of the flap and the mucosa formed a fine line of union (fig. 6). The ileostomy stoma now rested about 2 inches (5 cm.) beyond the abdominal wall.

PROSTHESIS FOR COLLECTION OF BOWEL CONTENTS

Any contact of ileal contents with the skin may result in excoriation of the latter, and, even though the intestinal contents drop into a bag

Fig. 6.—Condition about eight weeks after ileostomy. The mucosa extends beyond the skin just far enough to permit the easy fitting of the ileostomy cup (shown in figure 7) and thus prevents contamination of the skin with feces.

from a length of ileum, there is likely to be irritation of the skin near its junction with the mucosa.

With the help of Drs. Paul E. Richards and Robert E. Peters, of the Prosthetics Department of the Veterans Administration Hospital, Hines, Ill., we have devised a prosthesis which has met in part the requirements of a satisfactory "ileostomy cup."

The prosthesis consists of a basic form of sponge latex molded to the abdomen for a radius of approximately 7 cm. about the ileostomy and painted with three layers of pure latex to seal the pores (fig. 7). A firm acrylic resin mold is annealed over this, and at its peak there is a rounded cuff about 4 cm. in diameter (fig. 8). A rubber bag about 20 cm. in length snaps over the rim of the cuff and is held

in place by its own elasticity. The cuff has a solid floor except for an opening in the center which admits the mucosa only. The edge of this opening is lined with soft sponge latex to eliminate pressure on the mucous membrane and fits

Fig. 7.—Ileostomy cup constructed by the prosthetics department of the Veterans Administration Hospital. The outer hard frame is made of firm acrylic resin, and the inner core which fits about the ileostomy is sponge latex covered with pure latex to seal its pores and prevent soiling.

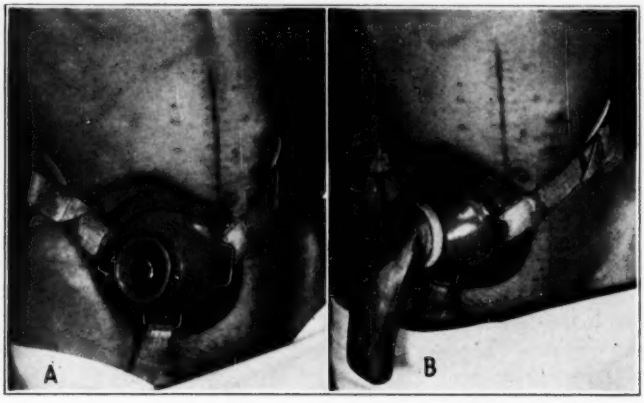

Fig. 8.—Ileostomy cup in place without (*A*) and with (*B*) disposable latex bag for the collection of fecal material.

closely about the mucosal edge. The floor of the hard plastic cuff is about 8 mm. below the rim. In order to keep the mucosal opening in place, the ileostomy is supported with cotton, wrapped about its base before the prosthesis is set in place.

A little zinc oxide ointment over the skin at its junction with the mucosa serves to seal the opening in the prosthesis. The appliance is held in place by a strap around the trunk and another through the groin.

During a peristaltic wave the ileostomy becomes relatively rigid and the stoma is forced against the prosthesis, acting further to maintain the seal and prevent soiling of the skin. The rubber bags are made by painting multiple layers of latex over plaster forms, and the patient carries a small supply for change and disposal at will.

The consistency of the ileostomy four months after its construction is that of a relaxed penis. It may be pulled from the abdominal wall 1 to 2 inches (2.5 to 5 mm.) beyond its apparent length. Such manipulation allows the patient to stimulate peristalsis at will and

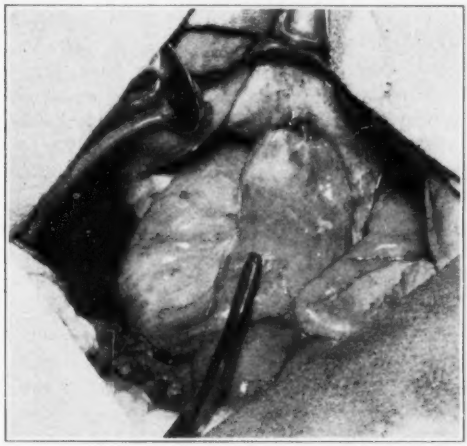

Fig. 9.—Photograph taken during the second operative procedure for removal of the remaining portion of the colon. The distal ileum is shown to have dilated to form an ampulla-like pouch in response to the loss of the colon.

empty the newly formed ampulla-like pouch of the lower part of the ileum (fig. 9), which was found to have developed when the second operation for removal of the remainder of the colon was performed. He has thus been able to halt the flow of intestinal contents for periods up to four hours, and it is hoped that the need for any kind of cup may eventually be eliminated. Certainly, the care of this ileostomy seems little more bothersome than that of the usual colostomy at four months.

COMMENT

Plastic surgeons and surgeons working on the hand have for years appreciated the valuable blood supply found in the broad-based

flaps from the abdomen. Shaw [2] has written an excellent description of the technic as applied to injured hands. The course of the superficial epigastric artery and vein as they come off the femoral vessels and pass upward in the skin and fascia of the abdominal wall assures an adequate blood supply to this area of skin. Except as the skin may be altered by scars, there is little reason to expect difficulty with the nourishment of such a flap. In the procedure here described the suture line of the flap must, by virtue of the course of the blood supply, lie on the dorsal surface of the tube. As a result, there may over a period of time be a tendency for the tube to be drawn dorsally. Such contraction may need correction by a Z-plasty, but there are adequate skin and subcutaneous tissue to allow such a procedure.

While this is not an overly laborious or time-consuming procedure, it seems to us that it should not be used when the patient is not in reasonably good condition. A patient who is acutely and severely ill with ulcerative colitis should not have this type of stoma constructed when ileostomy is being performed as an emergency and oftentimes life-saving procedure. The success of this procedure will depend on good wound healing, which the severely ill patient will seldom demonstrate. However, when an emergency ileostomy is done, it would be to the patient's advantage to have the opening placed near the midline so that the skin of the right lower quadrant would not be molested and thus be available for later use in revising the ileostomy along the lines described.

Though we have not had an opportunity to carry out such a procedure, we feel that in many cases in which the conventional ileostomy has already been made in the right lower quadrant, it would be possible to mobilize the ileum sufficiently to accomplish this operation in the left lower quadrant.

SUMMARY

A technic is described for constructing a permanent skin-covered ileostomy by wrapping the terminal ileum in a flap of skin, subcutaneous tissue and fascia, nourished primarily by the superficial epigastric vessels.

A suitable prosthesis has been devised which fits such an ileostomy and provides for satisfactory collection of bowel contents.

DISCUSSION OF PRECEDING PAPERS

DR. HAROLD LAUFMAN, Chicago: I should like to comment on the excellent work done by Drs. Hill and Saltzstein and their group. I have had some laboratory and clinical experience with tetraethylammonium chloride. When a vasodilating drug such as this is used in a patient with vascular occlusion, one logically expects

2. Shaw, D. T., and Payne, R. L., Jr.: One Stage Tubed Abdominal Flaps; Single Pedicle Tubes, Surg., Gynec. & Obst. **83**:205-209, 1946.

local dilatation to result. This is not always the case. Therefore, one is entitled to ask: Should I use the drug, or shouldn't I? Is is good or is it bad? Will it do harm, or will it do nothing? Tetraethylammonium is an interesting drug because it does some of all these things. It is both good and bad. The Michigan group, responsible for much of the preliminary pioneering work with this drug, has obtained therapeutic results in many forms of peripheral vascular disease as well as in hypertension. Their work with the drug in hypertensive patients has indicated that the more precarious the hypertension the greater the effect of the drug (Lyons, R. H.; Moe, G. K.; Neligh, R. B; Hoobler, S. W.; Campbell, K. N.; Berry, R. L., and Rennick, B. R.: Effects of Blockade of Autonomic Ganglia in Man with Tetraethylammonium, *Am. J. M. Sc.* **213**:315 [March] 1947). From these observations they formulated the concept that the greater the stimulation in the sympathetic ganglions, the greater would be the blocking effect of the drug.

In our work we found that this concept could not apply to the type of local ganglionic stimulation which results from acute vascular occlusion (Martin, W. B.; Laufman, H., and Tuell, S. W.: Rationale of Therapy in Acute Vascular Occlusions Based Upon Micrometric Observations, *Ann. Surg.*, April 1949). As a matter of fact, we found that no generally acting drug was capable of releasing local stimulation in sympathetic ganglions to the extent that was obtained by local procaine block. We were, therefore, delighted when Dr. DeBakey's article appeared (DeBakey, M. D.; Burch, G.; Ray T., and Ochsner, A.: The "Borrowing-Lending" Hemodynamic Phenomenon [Hemometakinesia], *Ann. Surg.* **126**:850-865 [Dec.] 1947), in which his group reported similar results.

We have arrived at a concept concerning the action of tetraethylammonium chloride in peripheral vascular occlusions which I should like to present. The concept set forth by the Michigan group is apparently tenable when the sympathetic tonus throughout the entire body is of almost equal magnitude, but it requires revision when it is applied to local vascular occlusions. We conceive that the drug by acting on all ganglions in the body has a lesser effect on those ganglions harboring a powerful stimulus from an occlusive irritant than it has on normal ganglions. This, in effect, would be a distribution of the action of the drug along "paths of least resistance." Thus, in an instance of acute vascular occlusion, the action of the drug would dissipate itself throughout the body without being able to "break through" the area in which it was most needed. If its action resulted in a general drop in blood pressure, a harmful effect could result in the area already suffering from a diminished blood supply. Also, if the drug is injected too rapidly and a lowering of the blood pressure ensues, the same effect may result. This was reflected in our measurements by a diminution in caliber of already spastic vessels.

Our concept is borne out by the experiences of Dr. Saltzstein's group in their intestinal experiments. When the bowel was strangulated or when the area was otherwise stimulated, the drug actually resulted in a lowering of the temperature of the involved area, or a reversal of effect, so to speak.

It is known that in acute occlusions of the extremity or in stimulations of ganglions due to acute pain, the drug will cause either no effect on that limb or an actual drop in temperature. We interpret this reversal of effect as a dissipation of the drug among unstimulated ganglions, and because of the principle of hemometakinesia, blood is actually drawn away from the local area and the local temperature drops.

However, in instances in which there is a collateral blood supply and that collateral blood supply comes from a higher area innervated through another ganglionic level, the drug will affect such collaterals by dilating them and pro-

ducing an increased blood supply to the part. The drug is not able to produce new blood vessels, but when vessels are present they can be dilated provided the circumstances just described exist. This apparently was the situation in the occlusion experiments of the aorta which were presented here. I understand some of the successful experiments were in pregnant bitches which had a large collateral blood supply to the lower extremity. In such instances it certainly is conceivable that the drug resulted in sufficient dilatation of the collateral vessels to result in a decent blood supply to the lower extremity.

I should like to hear some other comments from some of you here. What I have related is simply the result of our experience with this drug and the application of our concepts to explain what otherwise would seem to be paradoxic results. I should like to commend the work of this group in performing these experiments, because I think it is important to realize the limitations of any drug.

DR. J. T. REYNOLDS, Chicago: I should like to make a remark about the paper by Dr. Patton and Dr. Johnston concerning the treatment of hemorrhage from esophageal varices. Our problem has been that of treating a patient properly who was actually bleeding to death under our eyes. One can avoid the patients and say they are too sick for treatment, but such an attitude is not commendable. Patients who are bleeding actively should not be subjected to the operation of portocaval shunt during their hemorrhage because they are in poor condition and cannot tolerate such operation. Obviously, the use of the balloon that Dr. Patton suggested has very many merits. Unfortunately, we have not yet had the opportunity of using their tube. We used a tube with a balloon on it which we manufactured ourselves, and it was not effective. At operation we found that the patient continued to bleed after we had inflated the balloon, because the balloon had dropped down in the patient's stomach.

I was glad to hear the suggestion of adding thrombin above the large balloon because we have found that in some of our patients bleeding from gastric cancers the use of thrombin was distinctly helpful. It is probable that patients who are bleeding actively can be treated with this balloon tube until bleeding has stopped. After the bleeding has stopped and the patients are in better condition, the definitive portocaval shunt should be done.

From Dr. Julian's paper this morning, I think it is apparent that very soon we will have some sort of device that will be satisfactory to allow us to do portocaval shunt very safely. This of course presumes a patient who is in good condition.

DR. MAX M. ZINNINGER, Cincinnati: I should like to make just a few remarks about the paper by Dr. McClure and Dr. Brush on islet cell tumors in the pancreas. I have not had a wide experience with these, but they are very spectacular tumors, as he has indicated. For instance, in 1943 I saw a patient in her sixties, who was admitted to the hospital in coma. She was first thought to have a brain tumor because of the coma. It was finally learned that her blood sugar was 23 mg. per hundred cubic centimeters and it was found that the only way she could be kept out of coma was by putting a tube into her stomach and giving her glucose solution continuously. She was operated on, and a tiny tumor, less than 1 cm. in diameter, was easily found in the head of the pancreas, and removal of the tumor entirely cleared up her abnormal glucose metabolism. However, her brain was permanently damaged as a result of the continuous insulin shock.

In contrast, I should like to point out that some of these cells do not produce insulin at all. For example, in 1941 I operated on a rather large tumor of the

pancreas, which measured 6 by 8 by 12 cm. after fixation. This patient showed no abnormal glucose metabolism. Careful study of the tissue showed that the cells contained no alpha or beta granules but only delta granules, and that type of islet cell apparently does not produce insulin. This patient died in 1943, and there was widespread metastasis of tumor which was comparable in appearance to the original tumor.

Dr. James T. Priestley, Rochester, Minn.: I think, as we have just heard from the last discusser, that the patients who have hyperinsulinism constitute a very interesting group, and operation on these patients can be satisfactory and simple or rather difficult and disappointing.

If there is a single adenoma found, ordinarily it can be enucleated without much difficulty, and the patient gets along quite well. On the other hand, sometimes one can search from the tail to the head of the pancreas and back again two or three times and not find anything in the way of a tumor. Usually in those circumstances there is a small lesion embedded within the gland, of the same consistency as the pancreas, and even though one may visualize it by making an incision in the pancreas, it may be the same color as the normal pancreas and very difficult to recognize. I recall an instance when a portion of the pancreas was removed for such a lesion, and the pathologist brought the specimen back and said there was no tumor, having made a number of sections through the pancreas, but further search did reveal the tumor.

I think that there are one or two points that might be mentioned. In the first place, these tumors can be multiple. The incidence of multiple adenomas of the islands of Langerhans is quite small, but just because one is found in a certain portion of the gland does not mean that further search should not be made for another adenoma. We have had 1 patient in whom a malignant adenoma, a functioning tumor, of the islands was removed, and the patient was relieved, but he subsequently returned with recurrent symptoms of hypoglycemia and there were metastases.

Perhaps you would be interested in the patient referred to, in whom we did total pancreatectomy six or seven years ago. Ths patient is alive and leading a normal life today. About a year ago, which was approximately five and a half years after operation, we had the opportunity to study her in the metabolic unit, and, in contrast in some ways with the experimental animal, she showed no evidence of decreased liver function by any of the currently employed tests, despite the fact that she had not taken substitution therapy of any kind. She did, of course, show marked lack of internal and external pancreatic function, in that she required between 20 and 25 units of insulin a day, and the percentage of undigested fat and protein in the stool was abnormally high.

Dr. John R. Paine, Buffalo: Will Dr. Laufman tell us a little of the details of the regimen and how long he followed the regimen in making these sterile devascularized intestinal loops?

Dr. H. M. Elder, Montreal: I was greatly interested in Dr. Thieme's review of appendicitis and still more interested in the fact that he gives a great deal of credit to the use of sulfonamides. I think that perhaps is an attitude of mind which we should not permit ourselves always to drift into. It is so easy to credit any improvement to the antibiotics and then, perhaps, to neglect some of the other things. I was not quite clear as to how the sulfonamide was used, whether it was used in intraperitoneal implant or not. I should like information on that point. My own experience has been that the intraperitoneal sulfonamide implant has proved very disappointing in that it tends to be a bit of an irritant. I have

not been able to satisfy myself that the actual concentration of antibiotic locally was effective against organisms. I wonder whether possibly the change in the operative technic he mentioned, the changes which have come about over the ten year period in preoperative and postoperative care of patients, may not have more to do with the gratifying lowering of his mortality figures than the actual sulfonamide therapy.

Dr Charles G. Johnston, Detroit: I want to say a word in relation to the point which Dr. Reynolds brought out. I doubt that Dr. Patton made it clear. In the case which he reported operation was not done shortly after the patient was bleeding. We used the same principle in stopping the bleeding. It is purely a temporary measure. Its use is primarily that of stopping the blood. It is purely a matter of applying pressure on the dilated veins. What is done afterward is another problem. It is really a matter of tiding the patient over until something else can be done. Usually we feel that a portocaval shunt or some type of shunt which will reduce the pressure in the portal system is the ideal form of therapy if it is possible to do that afterward. As a matter of fact, so far as we are concerned, bleeding from the esophageal varices is the best indication and the most obvious indication for portocaval shunt.

Dr. Edwin M. Miller, Chicago: I wonder whether as a result of these injection experiments of Dr. Noer, in which after tying off the main artery as well as the arcades and the vasa recti the segment of bowel becomes filled with dye via the anastomotic vessels within the bowel wall, he could draw any conclusions which would in any way materially affect our standard procedures used in performing an end to end anastomosis of the intestine. After all, what we rely on after tying off the main vessels to a loop to be resected is the color changes in the bowel wall in order to determine where we can safely plan our lines of suture.

Dr. Brock E. Brush, Detroit: I want to thank Dr. Zinninger and Dr. Priestley for their interesting comments on this subject. I did not intend to convey the impression that all islet cell tumors are functional. According to Backus, 80 per cent are silent. Multiple tumors have been found in about 15 per cent of the reported cases. The histogenesis of these tumors is very interesting, as there are alpha, beta and delta cells and a tumor may arise from any of these. The group of suspicious tumors is of great interest because they appear malignant to the pathologist and to the surgeon and yet have had a rather benign course in many instances.

Dr. E. Thurston Thieme, Ann Arbor, Mich.: Although our hospital at Ann Arbor is in the bright light of a university hospital, we are rather inclined to take up new ideas slowly, because it is a small, private hospital. Therefore, the use of sulfonamides did not begin as early or on an experimental basis, and they were not used under any planned control. We never used the large doses in the peritoneum that were so frequently used and later reported with bad effects. We did use sulfonamides in the abdomen at the start, but such use was gradually discontinued and the drugs were used intravenously. Because of the divergency of the staff, there was no plan for the intravenous use. At the present time, if a sulfonamide is used, it is used intravenously as sulfadiazine. We did not use any sulfathiazole in the abdomen, which I believe was the cause of most of the difficulty. So there was no problem as far as that is concerned. I do agree that our newer methods, as we like to consider them, in the way of postoperative care and preoperative preparation of the patients had a great deal to do with improved results. However, in trying to review the variables, as I stated before,

it seemed that one outstanding benefit was the loss of peritonitis and abdominal abscess as the cause of death and increased morbidity. It is hard to know what to attribute this to, and, as the questioner stated, it is easy to give antibiotics credit. Perhaps we are wrong. I am not sure.

Dr. Rudolf J. Noer, Detroit: Dr. Miller has asked whether the demonstration of the efficiency of the anastomoses in the wall of the intestine has altered our concept of the technic of end to end anastomosis. I might answer that simply by saying no! It has been commonly taught that not more than 2 cm. of intestine can safely be denuded of its vessels. The demonstration of these anastomoses within the intestinal wall can give us more confidence when we are forced to put up with a greater amount of vascular deprivation, but we feel that in all types of anastomosis we should like to preserve all the blood supply that can possibly be conserved.

Dr. Harold Laufman, Chicago: Aside from the operation in stages, as we have described it, the only other points in the regimen consisted in giving the animal penicillin following the second operation for just three days. After the first stage, because the bowel was left open and washed out, it was not necessary to protect the animal any further. Thereafter, the animal was treated just as any animal would be after an operation on the gastrointestinal tract.

VARICOSITIES OF THE LESSER SAPHENOUS VEIN

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CHICAGO

THOSE varicose veins of the lower extremities which properly lend themselves to surgical correction arise largely as a result of intravenous valvular incompetency. Such relative or absolute incompetency occurs either entirely in the superficial vein or primarily in the deep and secondarily in the superficial vein. Owing to the force of gravity this anatomic defect leads to a venous reflux in the unsupported superficial veins with production of the well known stasis effects in the distal portions of the lower extremity.

Since the establishment of the concept of valvular insufficiency as a cause of varicose veins, it has been the custom to consider the phenomenon of venous reflux largely in reference to the saphenofemoral junction at the fossa ovalis. This view is due in part to the early teachings of Homans,[1] who pointed out the existence of the common and supposedly primary pathologic venous reflux at that point. With the passage of time, there have been a few modifications in his fundamental concept of ligation to correct the hydrostatic abnormality and thus to effect a more efficient rerouting of the venous return. The improvements have been due largely to the realization that the primary pathologic alteration is not actually located in the junctions which allow the venous backflow but is rather a matter of high valvular insufficiency in the iliac, femoral or even popliteal trunks. This insufficiency ranges from the functional inadequacy due to the demands arising from the upright position or the increased venous load from a pregnant uterus to the structural problem of complete absence of valves in some segments of vein.[2] Such anatomic, or rather embryologic, defects in the valvular pattern of the deep veins

From the Department of Surgery, Northwestern University Medical School.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Homans, J.: The Operative Treatment of Varicose Veins and Ulcers, Based upon a Classification of These Lesions, Surg., Gynec. & Obst. **22**:143, 1916.

2. (*a*) McMurrich, J. P.: The Valves of the Iliac Vein, Brit. M. J. **2**:1699, 1906. (*b*) Edwards, E. A.: The Treatment of Varicose Veins, Surg., Gynec. & Obst. **50**:916, 1934. (*c*) Eger, S. A., and Casper, S. L.: Etiology of Varicose Veins from Anatomic Aspect (Absence of Valves) Based on Thirty-Eight Adult Cadavers, J. A. M. A. **123**:148 (Sept. 18) 1943.

lead to the production of venous hypertension, which eventually becomes manifest in the superficial veins when a junctional restraining valve becomes secondarily incompetent. This relationship can be demonstrated easily on the operating table by asking the patient to cough, thereby suddenly increasing the intravenous pressure and dilating the saphenofemoral bulb under direct vision. On the other hand, it has been directly demonstrated by anatomic dissection on cadaver material by others [2c] as well as by workers in the laboratory of this university.[3] After the local restraining valve fails to function efficiently, it is only a matter of time before varicosities develop distal to that point in the superficial venous tree.

The large cross sectional area and location of the greater saphenous bulb lends itself well to being the commonest pathway for the development of superficial varicosities. Through a proper appreciation of the existence of valvular incompetence in the iliac and high in the femoral veins, a more logical attitude has arisen concerning the complete ligation of all the tributaries of the greater saphenous vein at the point of junction with the femoral vein. Such a procedure averts needless recurrences. In addition, it has proved illogical to assume that the heavy musculature of the thigh will sufficiently compensate for this high valvular inefficiency. Experience has shown that the venous hypertension eventually may render incompetent the valves of perforating veins, allowing the reflux to reach the superficial tree at some point or other, with the production of related varicosities. This fundamental concept has served to justify a more careful search for pathologic perforating branches lower in the thigh and leg. Anatomic studies have placed the discovery of incompetent perforators on a more predictable scale, with the result that they are not only more commonly sought out but also more accurately located and surgically corrected.[4]

LESSER SAPHENOUS VEIN

In a certain sense, the lesser saphenous vein could be catalogued as a perforator, but, because it is an established and constant anatomic entity, I prefer to consider it on a plane comparable with that of the greater saphenous vein in order that it may receive its rightful emphasis. There has been surprisingly little reference in the literature to the role played by the lesser saphenous vein in the production of varicosities in the lower leg. This perhaps is in part due to the fact that in 1934 Edwards, in his excellent paper on venous valvular anatomy, dismissed

3. Anson, B. J.: Personal communication to the author.

4. (*a*) Linton, R. R.: The Communicating Veins of the Lower Leg and Operative Technique for Their Ligation, Ann. Surg. **107**:582, 1938. (*b*) Sherman, R. S.: Varicose Veins, ibid. **120**:772, 1944. (*c*) Massell, T. B., and Ettinger, J.: Phlebography in Varicose Veins, ibid. **127**:1217, 1948.

the entire problem of primary incompetency of the lesser saphenous vein as largely nonexistent. Old and even recent monographs contain reference to the idea that varicosities located in the area of the lesser saphenous distribution are the result of the well known superficial collateral anastomotic connections with the greater saphenous system. There is no doubt that this type of secondary involvement of the lesser saphenous system does occur in a fair number of persons and that its correction follows multiple ligation of the greater saphenous system and disconnection of the two systems at the point of major communication. On the other hand, a mere passing mention of the possible existence of a primary reflux in the lesser saphenous system of veins has been made by Homans,[5] Linton [6] and Sherman.[4b] Sarma [7] reported an incidence of 0.5 per cent in 1,000 patients treated by ligation. In 1942, Heyerdale [8] stated that he thought that too much attention was being given to a search for incompetent perforators when a reflux from the lesser saphenous veins otherwise would explain the presence of varicosities in the lower leg. Two statistical studies [9] were reported shortly thereafter in which some interest in the problem was indicated by inclusion of a tabulation of the incidence of incompetency of the lesser saphenous vein, shown to be 3.8 and 7 per cent, respectively. My own first report [10] was made in 1946, describing personal experiences with this problem. A very recent report [11] on 452 operations on the lower extremities made no tabular reference to any procedure directed at the lesser saphenous vein. It is interesting to note that the last-mentioned authors admit an over-all recurrence rate of 21 per cent following what appeared to be adequate simple ligation of the greater saphenous vein, ligation combined with good retrograde sclerosis or ligation combined with proper stripping and phlebectomy procedures.

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5. Homans, J.: Circulatory Diseases of the Extremities, New York, The Macmillan Company, 1939.

6. Linton, R. R., and Keeley, J. K.: Postphlebitic Varicose Ulcer, Am. Heart J. **17**:27, 1939.

7. Sarma, P. J.: Saphenous Vein Ligation, S. Clin. North America **18**:129, 1938.

8. Heyerdale, W. W., and Anderson, E. M.: Diagnosis and Occurrence of Communicating Veins in the Treatmnt of Varicose Veins, Proc. Staff Meet., Mayo Clin. **17**:221, 1942.

9. Pearce, M. B.: Varicose Veins: Technique for Rapid Obliteration, Surgery **14**:901, 1943. Larson, R. A., and Smith, F. L.: Evaluation of Observations in Four Hundred and Ninety-One Cases of Varicose Veins, Proc. Staff Meet., Mayo Clin. **18**:400, 1943.

10. Carroll, W. W.: Venous Surgery, Quart. Bull. Northwestern Univ. M. School **20**:373, 1946.

11. McElwee, R. S., Jr., and Maisel, B.: Study of the Results of Surgical Treatment of Varicose Veins, Ann. Surg. **126**:350, 1947.

A review of our clinical experience indicates that in addition to the accepted incompetency at the saphenofemoral junction and the usual perforators in the thigh and lower leg, we have seen a substantial number of instances of primary venous reflux in the lesser saphenous vein. To date, in 515 lower extremities consecutively operated on, there were 60 instances of this type of reflux which necessitated ligation for correction. This represents an incidence of 11.6 per cent. Of these extremities, 44 were handled by ligation of the lesser saphenous vein alone, while in 16 instances ligation of the greater saphenous vein also was carried out because either of suspicion or of the actual presence of obvious incompetency in both systems. The remaining 450 extremities presented varicosities which were thought to arise entirely from the greater saphenous system. It is worth while to point out that of the 44 extremities subjected to the procedure of ligation of the lesser saphenous vein alone, 6 already had received ligation of the greater saphenous vein elsewhere. One might feel that these should be listed under the combined procedure, but it was apparent that little benefit had accrued from the previous operation; hence they were included in the group receiving ligation of the lesser saphenous vein alone. One might conclude from this fact that attention should routinely be given to the popliteal space in order to assess correctly the role played by the lesser saphenous vein in the production of the varicosities at hand.

ANATOMY OF THE LESSER SAPHENOUS VEIN

The anatomic course of the lesser saphenous vein undoubtedly has been the cause of previous failure to recognize its relationship to the varicosities under consideration. This vein drains the dorsum of the foot and the posterolateral aspect of the lower leg, to empty into the popliteal vein above the flexion crease of the popliteal space. In a few persons this vein progresses cephalad in the subcutaneous tissues, penetrating the fascia at some point in the lower portion of the popliteal space to enter the popliteal vein at a sharp angle (fig. 1). Assuming such a superficial course, one would suspect that any primary venous reflux through this route would result in varicosities located high in the posterior part of the calf, showing some externally evident relationship to this system of veins. It is our experience that such a relationship would be logical when this particular anatomic pattern exists, but, on the other hand, this pattern is not common.

The crux of the matter lies in recognition of the fact that the lesser saphenous vein penetrates the fascia at variable points lower in the calf and passes upward at a deeper level, well out of sight of the casual examiner's eye, to be found only by means of careful palpation. (If one keeps in mind this concept of venous reflux as the essential factor

in the production of varicosities, this point of penetration may well be referred to as the point of emergence.) This fascial penetration (or emergence), in our experience, is at a point between one third and two thirds of the distance from the popliteal crease to the ankle joint (fig. 1 *B*). As a result there is a critical area extending over one third to two thirds of the upper posterior aspect of the calf that usually is entirely free of evident varicosities when the primary reflux is located in the lesser saphenous system. In addition, it is possible because of the free anastomosis between the two systems in the lower leg that distal medial branches may be dilated and varicose from reflux from the lesser saphenous vein. In such circumstances, it may mistakenly

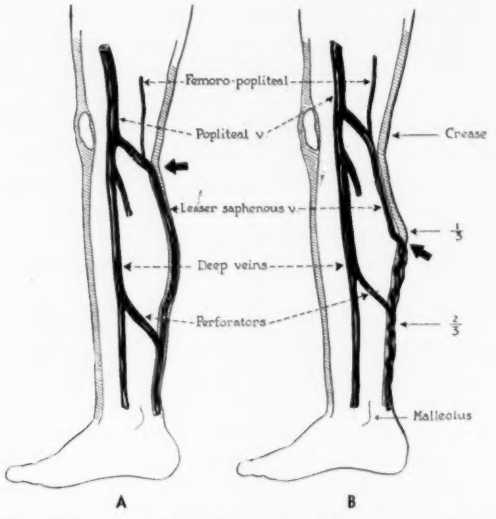

Fig. 1.—Superficial and subfascial course of the lesser saphenous vein. *A*, occasional pattern of fascial penetration; *B*, common pattern of fascial penetration.

appear that only the greater saphenous system is implicated, the lesser saphenous component being entirely overlooked. Anatomic dissections in our own laboratory as well as observations in the operating room have verified these clinical impressions, the vein occasionally being found to join the popliteal vein at a very high level.

METHOD OF EXAMINATION

After evaluation of the thigh has been completed, the lesser saphenous vein should be examined from the posterior aspect of the calf. With the patient standing on a high platform, it is important

first to ascertain from general inspection whether one might expect to find an incompetent lesser saphenous vein. A smooth upper calf with varicosities starting midway down and extending toward the heel and around to the lateral aspect of the ankle and dorsum of the foot should raise immediate suspicion (fig. 2). Any distal varicosities which seem to have no obvious relationship to the medial tributaries

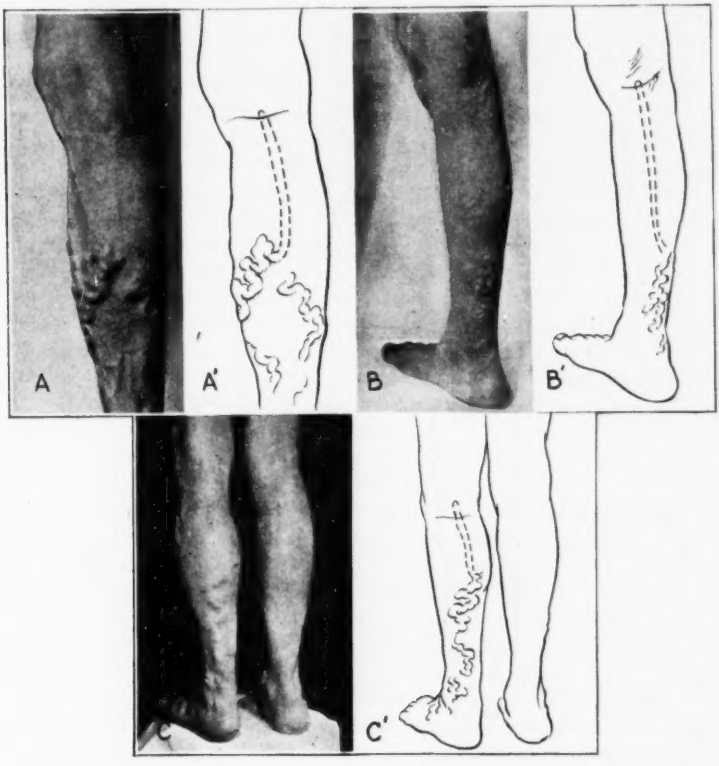

Fig. 2.—Varicosities resulting from primary venous reflux in the lesser saphenous system.

of the greater saphenous vein should be suspect. The third large group includes those which persist after previous adequate ligation of the greater saphenous vein, provided conclusive proof is present that there are no anteromedially located incompetent perforators. When the knee is slightly flexed and the weight is borne by the opposite extremity, there is sufficient relaxation of the upper calf and popliteal space for

the examiner to palpate for the vein. The normal vein cannot be palpated except in thin persons; hence if palpation at or just below the transverse crease in the skin results in the discovery of a firm venous trunk it must be considered significant. Repeated compression of the

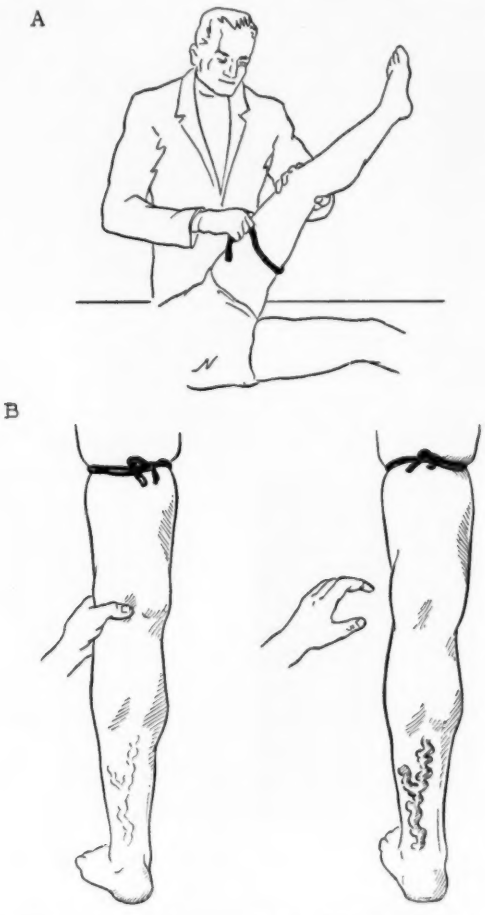

Fig. 3.—Thumb compression tourniquet test for evaluation of incompetency of the lesser saphenous system.

lower varicosities which communicate with this trunk may aid in finding the vein through the upward transmitted impulse (modified

Schwartz test). Once its discovery has placed the vein under suspicion, then the principles of the tourniquet tests can be applied.

With the proper use of soft rubber tubing constrictors, either single or multiple, the problem of detecting incompetent perforators in the thigh or calf is largely solved. In some persons this also may be sufficient for the lesser saphenous vein,[12] but I feel that this should not be relied on because of the fact that the vein lies well beneath the fascia and deep in the popliteal space, protected from circumferential compression by the hamstring tendons exactly at the point where the test should be most accurate. Because of this anatomic relationship, the application of the thumb is admirably suited to the purpose. The veins are emptied by elevation of the leg, and a section of soft rubber tubing is applied to the lower third of the thigh to secure control of any possible reflux through the greater saphenous system (if this is necessary). The popliteal space then is compressed with the thumb while the remaining fingers take a firm grip on the anterior aspect of the knee for stabilization of the compression (fig. 3). The patient then is allowed to stand, the thumb compression being maintained for twenty to thirty seconds. It then will be obvious that if the veins do not fill the source of the reflux has been found (fig. 3*B*). This is immediately verified by removing the thumb compression and noting that the varicosities immediately fill from above downward. The tourniquet around the thigh is left in place to eliminate the possibility of any greater saphenous reflux throughout this procedure.

TREATMENT

The principle of ligation for correction of varicosities of the lesser saphenous vein applies exactly as it does to any perforator in the thigh or lower leg. The lesser saphenous vein lends itself well to proper ligation at the point of junction with the deep system in much the same way as does the greater saphenous vein. As in other instances, we have found it convenient to mark the longitudinal course of the subfascial trunk, even though the transverse incision across the popliteal space is used. The transverse incision is more physiologic and anatomic; it heals well and allows for adequate exposure of the vein and its branches. It must be placed about 1 to 3 cm. above the crease because the vein always enters the popliteal vein at a point higher than physical examination would suggest. In the event that the incision has been placed too low, it can be extended upward at its lateral end in the form of an "L" or merely lengthened both medially and laterally to afford sufficient retraction of the skin. The well defined fascia can be incised

12. Steiner, C. A., and Palmer, L. H.: Simplification of Diagnosis of Varicose Veins, Ann. Surg. **127**:362, 1948

either transversely or longitudinally as desired (fig. 4). The tibial nerve and its posterior femoral cutaneous sensory branch should be carefully retracted to avoid injury. In addition to the main trunk joining the popliteal vein, there usually will be found at this point an upward continuation known as the femoropopliteal vein which empties either into the femoral vein at a higher level or, more commonly, into the profunda femoris vein. This must be ligated not only to prevent reflux which might develop later but also to aid in complete mobilization of the saphenopopliteal junction point for the highest possible ligation (fig. 4*B*). An occasional connection with the greater saphenous vein also is found at this level. In the depths of the wound there occasionally is found a direct perforating branch between the lesser saphenous and

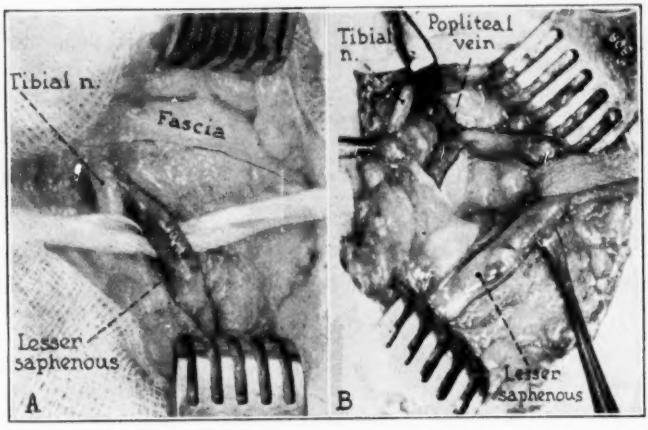

Fig. 4.—Photographs made at operation. *A*, fascia incised transversely showing close relationship of enlarged lesser saphenous vein to tibial nerve. *B*, junction of lesser saphenous and popliteal veins with tibial nerve retracted.

the deep system 1 or 2 cm. distal to the main junction. This may connect with one of the venae comites below their point of fusion to form the popliteal vein. Such a perforator also must be ligated and divided when present. In cases of doubt concerning the existence of other, more distal, perforating connections with the tibial vessels, a short longitudinal incision can be made at the point of fascial emergence. This will facilitate exploration and in some instances may allow the entire subfascial trunk to be excised if desired. Excision of the adjoining large superficial varices also is in order, whereas distal injection with sclerosing solution can be performed for small branches if desired and if not otherwise contraindicated.

Immediately after operation, the patient should be encouraged to walk as after any other venous ligation. A firm elastic roller from the toes to the lower thigh will be of help for temporary vascular support as well as to add compression to the healing wounds. The patient may wish to walk with the knee slightly flexed for the first day or two, a mechanical adjustment which certainly does not hinder good healing of the wound. Women may be requested to wear a higher-heeled shoe on the treated side to achieve this slight flexion for the sake of comfort and to prevent undue tension on the wound.

When ligation of the great saphenous vein also is planned for the same leg, I have found it expedient to postpone the procedure in the groin until another time.

RESULTS

Follow-up analyses of patients who have had surgical correction of varicose veins frequently fail to take into account many of the adjunctive measures necessary for a satisfactory result. The anatomic study and the procedures herein described constitute merely a small but significant part of the entire diagnostic and therapeutic program for such patients. Appreciating this fact, I do not wish to report a "success story." Suffice it to say that the results have been most gratifying. A considerable degree of alleviation of the distal venous stasis effects has been achieved, as would be expected to follow elimination of as much as possible of the pathologic venous reflux. When the location of the latter has been in doubt, we have for some time found phlebograms to be of great help, especially after the ordinary levels have been surgically explored. There is no one operation which will solve the problems of all these patients, but thorough unbiased evaluation of each extremity may result in fewer therapeutic failures.

SUMMARY

In 515 extremities presenting varicose veins secondary to valvular insufficiency, there were 60 instances of primary venous reflux in the lesser saphenous system.

Ligation of the lesser saphenous vein and its tributaries at the popliteal junction corrects this pathologic reflux and effects a more efficient rerouting of venous return.

A clinical test is described which has been of value in localizing this reflux through the saphenopopliteal junction.

SUBSTITUTION OF THE URINARY BLADDER WITH AN ISOLATED SEGMENT OF SIGMOID COLON

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AND
H. HARPER KERR, M.D.
OMAHA

THE PRESERVATION or restitution of normal function, although not always essential, is certainly the most desirable goal to be attained after any surgical procedure. In this respect, all operations for total removal of the urinary bladder fail. This does not imply that the present modifications of the Coffey operation [1] are not satisfactory, for there is much evidence to the contrary, but it does imply, rather, that these operations do not attain the ideal of restoring the normal route of urinary excretion.

Assuming that it was possible to preserve bladder function and to use an isolated segment of sigmoid colon as a substitute bladder, we planned a two stage operation and carried it through to completion in 5 of the 7 dogs in which it was attempted. There were 4 females and 1 male. The results obtained in the first 2 animals were reported in 1943.

The technic of the operation, previously reported,[2] is outlined in the drawings in figure 1.

. . . It was performed in two stages. At the first stage the right ureter was divided at its junction with the bladder and dissected from its bed sufficiently to allow its transplantation to a loop of the sigmoid which had been selected to replace the bladder. The most proximal portion of the sigmoid which could be carried down to the position of the bladder without tension was selected. The ureter was transplanted by means of a strangulation suture at the head of a 1.5

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Coffey, R. C.: Production of Aseptic Uretero-Enterostomy by a Suture Transfixing Ureteral Wall and Intestinal Mucosa, J. A. M. A., **94**:1748 (May 31) 1930; Transplantation of Ureters into Large Intestine by Submucous Implantation, ibid. **99**:1320 (Oct. 15) 1932; Further Studies and Experiences with Transfixion Suture Technic (Technic No. 3) for Transplantation of the Ureters into Large Intestine, Northwest. Med. **32**:31 (Jan.) 1933.

2. Bisgard, J. D.: Substitution of the Urinary Bladder with a Segment of Sigmoid, Ann. Surg. **117**:106-109 (Jan.) 1943.

cm. submucosal bed, as described by Coffey in his revised aseptic technic. Four or five centimeters above this point, the sigmoid was divided between clamps with a cautery. The distal end was closed aseptically with two rows of sutures and dropped into the pelvis. The proximal end was brought out through the wound as a temporary colostomy. The abdominal wall was closed around the exteriorized proximal end, the clamp removed, and the free edge of the bowel sutured to the skin around its circumference. Within three or four days liquid stools were passed by rectum. On the 10th postoperative day, and for four days subsequently, the blind pouch of rectum and distal sigmoid was irrigated with salt solution

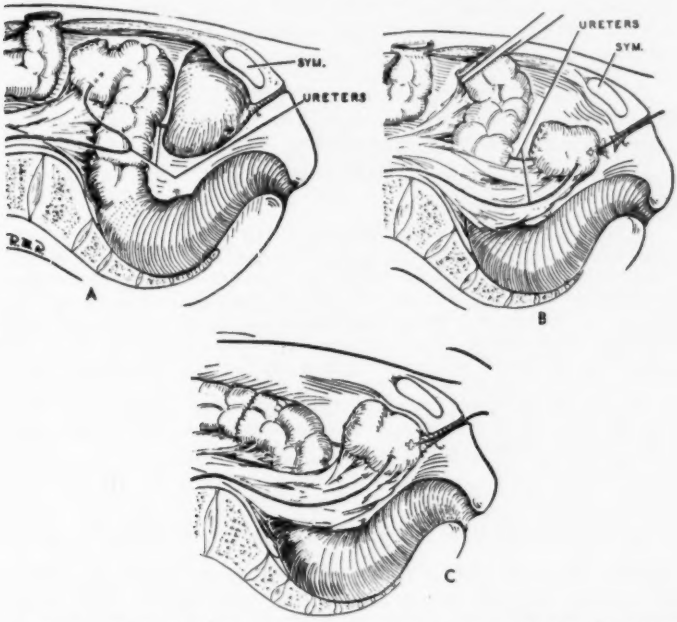

Fig. 1.—At the first stage (*A*) the right ureter is transplanted to the segment of the sigmoid colon which will subsequently be utilized as a substitute bladder. The bowel is divided above this point, the distal end infolded and the proximal end exteriorized as a colostomy. *B* and *C* show the steps of the second stage; *C* the completed bladder, transplantation of the left ureter, isolation of the sigmoid bladder and suture of its distal free end to the urethra and reestablishment of continuity of the colon. (Reprinted with permission of J. B. Lippincott Company from Bisgard, J. D.: Substitution of the Urinary Bladder with a Segment of Sigmoid, Ann. Surg. **117**:106 (Jan.) 1943.

until the solution returned clear [in an endeavor to render it relatively sterile for the second operation].

On [or soon after] the 14th day the second stage was performed. This consisted of the following steps: The left ureter was divided at its junction with the bladder dissected from its bed and laid aside. The bladder was then resected

and a small mushroom catheter threaded through the urethra from within out, with the mushroom-end remaining in the peritoneal cavity. The distal sigmoid was divided about 4 to 6 cm. distal to the site of previous ureteral implantation. The mushroom tip of the catheter was inserted into this isolated segment of sigmoid and secured within the lumen with a purse string suture placed around it about 1 cm. above the free edge. With traction applied to the catheter beyond the meatus by an assistant, the open end of the isolated pouch of sigmoid was drawn down to the cut end of the urethra and the two edges approximated with interrupted mattress sutures. The left ureter was then placed in a submucosal bed and implanted directly into the lumen of the pouch. [In all but 2 animals] the colostomized, or proximal end of the sigmoid was dissected free from the abdominal wall and the continuity of the bowel reestablished by an end to end anastomosis between it and the free end of the distal sigmoid.[2]

In 2 animals the bowel was not anastomosed, but, rather, the proximal end was left exteriorized as a permanent colostomy for studies of motor function. After the abdomen was closed, the catheter was cut off at the urethral meatus and fixed to the meatus with a suture. Five days later it was removed.

By dividing the operation into two stages, two important objectives were accomplished. Continuous urinary excretory function was assured. The success of the first ureteral transplant was established before disturbing the other ureter, thus avoiding the hazard of anuria. By diverting the fecal current through the temporary colostomy, and as a result of irrigations, the distal pouch was rendered relatively aseptic. This made it possible to isolate the segment of sigmoid and to carry through the rest of the operation with but slight risk of peritonitis.[2]

All 5 dogs remained well and appeared to be normal until they were killed to obtain specimens. Two were killed at four months after operation, 1 at one year and 2 at two years.

RESULTS

The results of the experiments may be summarized briefly as follows.

Continence.—In all animals urinary continence developed within a day or two after the removal of the urethral catheter. Periodically throughout the life of the animals catheterizations were done, and never was there more than 2 ounces (60 cc.) of urine recovered. Often the bladder contained less than ½ ounce (15 cm.). Before the catheter was removed, 2 ounces of water was instilled and in every instance it was retained for fifteen minutes or longer.

In 2 dogs the quantity and frequency of urination was measured. This was accomplished with the animals in drainage cages, all urine draining from the floor of the cage into a receptacle equipped with a float with a writing arm which inscribed a quantitative record on a smoked drum. One of these records appears in figure 2. In both animals urination occurred at intervals of fifteen to forty minutes and in quantities varying from 15 to 35 cc.

Voluntary Urination.—The extent of voluntary control of the substitute bladder could not be definitely determined. The females squatted to urinate, but the male was usually unable to expel urine when he made the usual gesture toward trees and posts.

The motor activity of the sigmoid bladder was investigated in 2 animals by means of indwelling inflated balloons connected to a manometer which inscribed a kymographic record of the peristaltic activity. One of the records is reproduced in figure 3. It is apparent that the rhythmic contractions and the segmental peristaltic waves normally

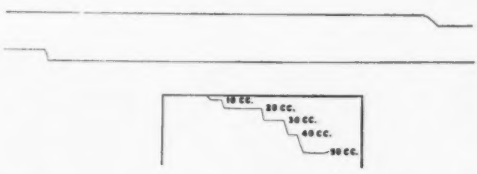

Fig. 2.—A kymographic recording of urinary output during an interval of eighty minutes. During this period the dog urinated approximately 25 cc. on two occasions.

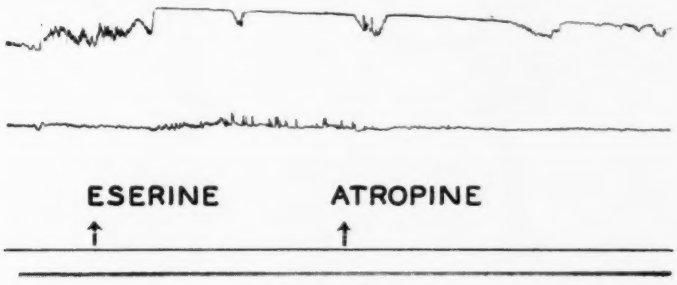

Fig. 3.—Simultaneous kymographic tracing of the motor activity of the isolated segment of sigmoid used to replace the bladder (upper one) and of the colostomized descending colon (lower). The records were obtained by means of indwelling inflated balloons. Note that in both tracings eserine produced a tonic motor response and atropine, mild inhibition; also note the preliminary record of normal rhythmic and segmental contractions.

observed in the colon remained unaltered despite the change of function. Eserine increased tonicity to the point of spasm, a much more vigorous response than that registered simultaneously by a balloon passed into the colon through the colostomy. Atropine in both segments produced the usual antagonistic (inhibitory) response.

Urinary Infection.—At no time was there subjective evidence of infection of the urinary tract in any of the animals. However, no bacteriologic studies were done. In repeated examinations of the urine at varied intervals after one month following operation there were no abnormalities discerned. The centrifuged sediment invariably contained a few pus cells, but there was never gross pyuria. Furthermore, there was no evidence at postmortem examination that an infection of the urinary tract existed or had ever existed. In all 5 animals the kidneys, ureters and sigmoid bladder were normal in appearance. There was no dilatation of the ureters and of the pelves of the kidneys. Microscopic examination of the segment of sigmoid showed a normal colon

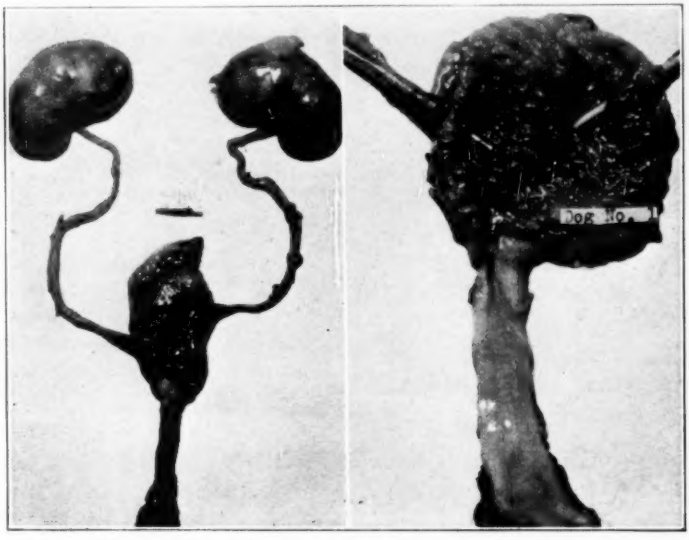

Fig. 4.—Postmortem specimen. The kidneys and ureters are normal. In the open sigmoid bladder and urethra note line of union, also, probes in the ureteral orifices. (Reprinted with permission of J. B. Lippincott Company from Bisgard, J. D.: Substitution of the Urinary Bladder with a Segment of Sigmoid, Ann. Surg. **117**:106 (Jan.) 1943.

histologic picture. It had not been altered with a change of function even after two years.

SUMMARY

A two stage operation for resection of the bladder and for its replacement with an isolated segment of sigmoid colon is presented. The operation was performed successfully in 5 dogs, and in each instance the substitute bladder functioned satisfactorily. In no instance was there evidence of infection of the urinary tract.

CONCLUSION

The success of this operation in animals raises the question of its applicability to problems encountered in man. First, it is a much more formidable procedure than the Coffey type of operation, and it is very doubtful that the possible advantages that it might give would compensate the increased operative risk except for benign lesions necessitating total removal of the bladder. In extrophy, practically the only lesion of this type, the open exteriorized urethra makes the operation impossible.

In malignant disease adequate resection often includes a portion of the urethra (including the prostate gland in the male) and with it the prospect of loss of continence.

REDUCTION IN MORTALITY AND LOSS OF LIMBS IN DIABETIC GANGRENE AND INFECTION

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AND
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IN 1939 a study was made of the amputations done for diabetic gangrene and infection at the Buffalo General Hospital during the preceding seven years. The mortality for all cases was 35 per cent and for major amputations, 41 per cent. A review of the literature showed that these were not comparatively high figures, although a few centers were beginning to report reduction in mortality through methods aimed at quick riddance of infection. There had been no significant reduction in the mortality in this hospital during the seven years covered by the study. Analysis disclosed that in 75 per cent of all our cases there was some infection of the stump or amputation site. In all the fatal cases postoperative infection had been present.

It seemed, then, that postoperative infection played the major role in maintaining the high mortality rate. The factors of age, blood supply and severity of diabetes appeared much less important, though, of course, it was recognized that adequate medical management in cooperation with surgical treatment was essential. In order to reduce the incidence of infection, during the next few years a two stage amputation was done in cases of severe infections necessitating major amputations. The first stage consisted of a guillotine amputation through the midcalf to eliminate all infected tissue; no attempt at closure was made at this time. A definitive supracondylar amputation was done later when the guillotine stump was clean and the patient's general condition had improved. In a number of these cases cultures taken from the apparently healthy muscle at the time of the guillotine amputation yielded the same organisms as were cultured from the infected foot. However, only 1 of a series of 28 patients so treated had any evidence of infection in the stump of the definitive thigh amputation, and that

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was a minor infection. There was only 1 death, too, in this series and at autopsy the patient was shown to have a massive pulmonary embolism from a mural thrombus in the heart. This was a remarkable reduction in mortality and incidence of postoperative infection. The mortality for all cases during the five year period 1940 to 1944, inclusive, was 8.8 per cent, and that for cases in which guillotine amputation had been done was 3.5 per cent (table 1). The use of sulfonamide drugs

Fig. 1.—Amputation of first and second toes and metatarsal heads for gangrene. Skin graft completely healed. Photograph five months after amputation.

TABLE 1.—*Comparative Mortality by Periods*

Period	Cases, Number	Deaths, Number	Mortality, Percentage
1933-1939	140	49	35
1940-1944	136	12	8.8
Guillotine	28	1	..
1945-1948	122	5	4.1

during this period was an additional factor, though they were not used routinely, especially during the early part of the period.

In 1943 some badly infected feet were treated by local amputation and débridement of all infected tissue, as had been described earlier by Zierold,[1] rather than by guillotine amputation. Often the amputation site so treated became covered with such healthy-looking granulations that it was decided to cover some of them with skin grafts. Early in 1945 penicillin began to come into general use, and, with its use, it became safer to do local amputations, with less fear of danger from spreading infection. From this time on the procedure of local amputation and débridement was carried out in steadily increasing numbers of cases, with less and less regard to the status of the local blood supply. At the present time most of our major amputations are done

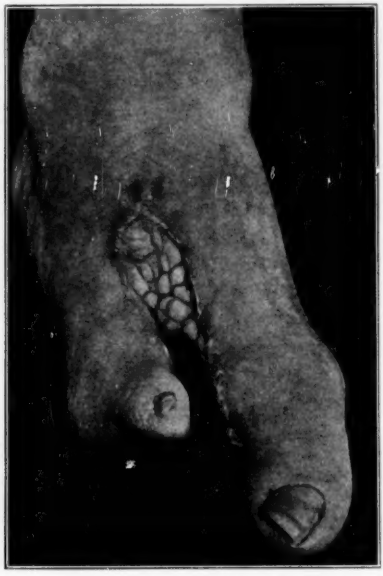

Fig. 2.—Wedge amputation of second, third and fourth toes done for severe spreading infection and cellulitis of foot. Photograph four weeks after grafting.

in cases in which a local amputation has failed to heal because of poor blood supply. As would be expected, the most favorable cases for local amputation are those that still have a comparatively good blood supply. Yet feet with apparently very poor blood supply often heal remarkably well, and a few of our best results are in patients who had local amputations only because they refused a major amputation.

1. Zierold, A. A.: Gangrene of Extremity in the Diabetic, Ann. Surg. **110**:723-730 (Oct.) 1939.

As shown in tables 2 and 3, during the four year period 1945 to 1948 70 per cent of all amputations in diabetic patients were local amputations and only 30 per cent were amputations through the leg or thigh. During the period 1933 to 1939 these figures had been reversed, 71 per cent of all the amputations being through the thigh and 29 per cent local. During the past four years 86 per cent of our amputations of toes and local amputations have been successful. By that we mean that they have ended in healing or the stumps have taken skin grafts successfully and a subsequent major amputation has not been required. It is readily apparent from these figures that we are now saving a large number of limbs which would formerly have been lost through major amputations.

TABLE 2.—*Distribution of Amputations by Period and by Type*

Period	Type of Amputation			
	Toe, Percentage	Leg, Percentage	Guillotine and Thigh, Percentage	Thigh, Percentage
1933-1939	29	...	..	71
1940-1944	50	4.4	21	25
1945-1948	70	4.9	6.5	18

TABLE 3.—*Results in Local Amputations**

Period	Cases, Number	Successful Results, Percentage
1933-1939	41	46
1940-1944	68	63
1945-1948	86	86

* Amputations of toes and of part of the foot.

The successful treatment of the diabetic patient with gangrene or infection of the extremities depends on a number of factors, high among which stands close cooperation between the surgeon and the internist. Without the best possible medical management of the diabetes and its complications relatively little can be accomplished by operation alone. In many of our cases with gangrene and impending or actual coma, strenuous treatment by the internist has brought the situation sufficiently under control to allow surgical intervention within a few hours following the patient's admission to the hospital.

Our present procedure consists in (1) close cooperation between internist and the surgeon in caring for the patient as well as for his gangrene, (2) use of large doses of penicillin and other antibiotics as indicated to bring infection under control and (3) early and complete local amputation and débridement of gangrenous infected tissue. The type of operation is selected to allow no barrier to remain at

the amputation site which might cause the collection, or interfere with the drainage, of pus and infected exudate. Amputations of toes and parts of the foot are either true guillotine procedures or of the "wedging" or guttering type, the surfaces being so arranged as always to allow complete dependent drainage with the patient in bed. Wet dressings are used only in case of good blood supply. In cases in which the blood supply is poor, bland ointment dressings are used and the entire extremity kept wrapped in thick layers of cotton batting and flannel bandage. When the area shows healthy granulations

Fig. 3.—Amputation of second toe and metatarsal head for osteomyelitis and perforating sinus. Photograph two weeks after application of pinch grafts.

on the surface, it is covered with small pinch grafts taken from the same or the opposite thigh. Pinch grafts are used because of their ability to take almost universally in spite of adverse conditions. In our hands, they have given well covered, satisfactory surfaces. Care must be taken not to apply too much pressure in dressings covering the grafts and to avoid pressure on other parts of the foot, especially in case of badly compromised circulation.

The kind of foot that the patient has left after this procedure depends on the extent of local amputation and débridement necessary.

Fig. 4.—Bilateral amputation of forepart of foot for gangrene following exposure to cold. Photograph nineteen days after amputation, nine days after application of grafts.

Fig. 5.—Amputation of most of lateral portion of foot for spreading infection with deep slough. Much of the area has healed by scarring, and the rest is covered with pinch grafts.

After single or multiple amputations of toes without extension into the metatarsal area, they are almost always good walking feet. After the more extensive amputations something is often left to be desired, by orthopedic standards. In many of our cases there has not yet been sufficient time for follow-up study, but in those that have the results have been encouraging. Even poor-looking feet often make good weight-bearing stumps. There is a tremendous difference in the patient's psychologic reaction to a local and to a major amputation. Finally, since most diabetic patients who have a major amputation never learn to use a prosthesis satisfactorily, saving a limb often saves the patient from complete invalidism.

SUMMARY

A survey of amputations for diabetic gangrene and infection at the Buffalo General Hospital from 1933 through 1948 is presented.

Mortality has been reduced from 35 per cent to 4.1 per cent.

The present procedure for local amputation is described. Local amputations now comprise 70 per cent of the total number, whereas amputations through the thigh formerly were 71 per cent of total.

In 86 per cent of local amputations there has been successful healing.

A large number of extremities are now being saved which would formerly have been lost through major amputations.

PROMPT POSTOPERATIVE ACTIVITY AFTER HERNIOPLASTY

Its Influence on Incidence of Complications and Rate of Recurrence

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MANY POSTOPERATIVE complications are favorably affected by prompt ambulation and other accelerated modifications in traditional convalescent care. On the contrary, the incidence of thrombosis in the deep veins of the lower extremities and of pulmonary infarction due to small, nonfatal emboli is unaltered.

Wounds heal kindly, and the rate of recurrence following hernioplasties of all types is significantly less among promptly ambulatory patients than among those who remain inactive in bed for ten to fourteen days after operation.

The data herewith submitted are offered in support of these assertions.

CLINICAL MATERIAL

The study is based on a critical survey of all the cases in which hernioplasty was performed at the Mary Imogene Bassett Hospital during the sixteen years from 1933 through 1948. These include cases of inguinal, femoral, epigastric, umbilical and ventral hernias, various combinations of these with inguinal ruptures, diaphragmatic and internal hernias and 2 cases of abscesses in inguinal sacs; a total of 467 operations was done (table 1).

These have been grouped according to the rapidity of postoperative mobilization of the patients. "Prompt" activity connotes arising from bed and walking within twenty-four hours after operation, occasionally during the afternoon or evening of the same day, never from the table to bed as advocated by some surgeons; "early" refers to ambulation commencing on the second, third or fourth day; "late" applies to mobilization which is not undertaken until the fifth day or after, usually on the tenth or twelfth postoperative day. No attempt has been made to grade the activity of "children"; this category includes all those from birth through 12 years of age.

There has been no selection of patients for specific plans of postoperative activity. Early ambulation was instituted in this hospital in 1940. The patients on whom hernioplasty was performed prior to that year remained in bed for traditional periods of convalescence, depending on the age of the patient and the type of hernia. During 1940 recumbency of two, three or four days only was allowed. Since 1941 all patients have been mobilized within twenty-four hours after hernioplasty, except for a very few in whom there were obvious and definite contraindications. These include acute postoperative coronary thrombosis, cerebral

From the Department of Surgery of the Mary Imogene Bassett Hospital.
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thrombosis or hemorrhage with paralysis of the lower extremities and peritonitis of bacterial origin secondary to perforation of the intestine by strangulation.

Three hundred forty-six hernias in this survey were unassociated with preoperative complications (table 2). The mortality in this group was 0.6 per cent.

TABLE 1.—*Tabulation of the Types of Hernioplasties in This Study*

	Patients					
	Adults Ambulation					
Hernioplasties	Prompt	Early	Late	None; Postoperative Death	Children	Total
Unilateral inguinal	161	12	97	5	53	328
Bilateral inguinal	27	0	5	1	5	38
Unilateral femoral	12	6	15	3	0	36
Umbilical	5	1	6	0	13	25
Epigastric	1	0	6	0	0	7
Postoperative ventral	7	2	9	1	0	19
Post-traumatic ventral	0	0	1	0	0	1
Inguinal and umbilical	1	0	0	0	0	1
Inguinal and postoperative ventral	1	0	1	0	0	2
Inguinal and unilateral femoral	1	0	2	1	0	4
Inguinal and bilateral femoral	0	1	0	0	0	1
Diaphragmatic	1	0	1	0	0	2
Internal	0	0	1	0	0	1
Abscess in inguinal sac	0	0	0	2	0	2
Total	217	22	144	13	71	467

TABLE 2.—*Associated Preoperative Complications*

	Patients					
	Adults Ambulation					
Complications	Prompt	Early	Late	None; Postoperative Death	Children	Total
None	175	13	98	2	58	346
Incarceration of omentum	7	0	12	0	1	20
Incarceration of intestine or colon	6	0	5	0	4	15
Incarceration of omentum and intestine or colon	3	0	2	0	0	5
Incarceration of intestine with obstruction	8	0	7	3	1	19
Incarceration of acutely inflamed appendix	1	2	0	0	0	3
Incarceration of tube and ovary	0	0	0	0	1	1
Incarceration, organ not stated	0	0	0	0	2	2
Strangulation of omentum	3	1	4	0	0	8
Strangulation of intestine with obstruction	12	5	14	5	4	40
Strangulation of omentum and intestine with obstruction	1	1	2	1	0	5
Strangulation of appendix epiploica	1	0	0	0	0	1
Abscess due to Escherichia coli in hernial sac	0	0	0	2	0	2
Total	217	22	144	13	71	467

Death in 1 case was due to massive pulmonary embolism, and in the other to peritonitis resulting from perforation of the sigmoid by a needle and suture in the repair of a sliding hernia. One hundred and twenty-one, or 26 per cent, were associated with incarceration or strangulation of some organ or viscus and fre-

quently further complicated by intestinal obstruction (table 2). Operation was considered urgent in these cases and performed as an emergency. Eleven of the 13 deaths occurred in this group, a mortality of 9.1 per cent. The average age of the patients who died was 60.3 years.

TABLE 3.—*Postoperative Complications*

Complications	Number				
	Adults Postoperative Activity				
	Prompt	Early	Late	Children	Total
Local					
Hematoma in wound, cord or scrotum *	21	1	6	3	31
Seroma in wound	2	0	1	0	3
Infection of wound	3	0	5	3	11
Cellulitis of abdominal wall	0	0	1	0	1
Discharge of nonabsorbable sutures	2	1	3	2	8
Stitch abscess	0	0	1	0	1
Disruption of wound (laparotomy)	29	2	18	8	57
Total					
Cerebral					
Cerebral thrombosis with hemiplegia	0	0	1	0	1
Cerebral hemorrhage, suspected	0	0	1	0	1
Total	0	0	2	0	2
Cardiac *					
Anginal attacks	0	0	1	0	1
Coronary thrombosis, with infarction of myocardium	0	0	2	0	2
Decompensation with pulmonary edema and congestion	0	0	2	0	2
Total	0	0	5	0	5
Pulmonary					
Bronchitis	8	0	9	0	17
Bronchopneumonia *	4	2	12	1	19
Partial atelectasis *	8	0	5	0	13
Massive atelectasis *	0	0	2	0	2
Infarct of lung, demonstrable or suspected	8	1	7	0	16
Pulmonary embolism, actual or suspected *	0	0	5	0	5
Pleurisy	1	0	4	0	5
Cough, unexplained	4	1	4	0	9
Total	33	4	48	1	86
Vascular					
Thrombophlebitis, superficial or deep	1	0	2	0	3
Thrombosis of deep veins of legs, actual or suspected *	15	1	9	0	25
Thrombosis of intrinsic vessels of male genitalia	0	0	1	0	1
Embolism of femoral artery	1	0	0	0	1
Total	17	1	12	0	30
Gastrointestinal					
Persistent hiccup	2	0	3	0	5
Dilatation of stomach *	1	0	6	0	7
Persistent abdominal distention *	5	0	16	0	21
Total	8	0	25	0	33
Genitourinary					
Postoperative inhibition of bladder					
Necessitating 1 catheterization only *	15	3	4	0	22
Necessitating 2 or more catheterizations *	9	5	27	0	41
Cystitis	2	4	5	0	11
Total	26	12	36	0	74
General					
Fever of unknown origin *	2	0	7	4	13
Total complications	115	19	153	13	300
Total operations	217	22	157	71	467
Incidence of complications (percentage)	53%	86%	98%	18%	64%

* Complications of some significance, discussed in the text.

POSTOPERATIVE COMPLICATIONS

All the patients have been under my personal care, supervision or observation. All the hospital charts and records have been carefully reviewed and special attention paid to symptoms and signs which

suggest or indicate complications during convalescence. The number of patients who were first mobilized on the second, third or fourth day ("early") is too small to be of statistical significance, and complications in children, who are never quiet during convalescence, are too infrequent to justify consideration. Consequently, this survey is limited to a comparative study of the complications which occurred among the adult patients who were activated within the first twenty-four hours ("prompt") and those who remained in bed for an average period of 10.8 days after operation ("late"). The two groups are fairly comparable in size, 217 operations in the first and 157 in the latter (table 3).

All complications have been classified according to the system involved and are recorded in table 3. The incidence of many is unaffected favorably or adversely, by the rapidity of mobilization of the patient during convalescence. Others are very definitely influenced by prompt activation. The complications of significance are designated by an asterisk in the tabulation and discussed in some detail in succeeding paragraphs.

Local Complications.—Hematoma in the wound, cord or scrotum was three and one-half times as common among the patients who were out of bed and walking within twenty-four hours as among the others. All wounds were dry when closed; hence it seems probable that prompt ambulation is conducive to postoperative oozing from tiny vessels which were not bleeding during the operation. Unusually careful hemostasis is imperative when such activity is permitted.

Cardiac Complications.—It may or may not be important that all the cardiac complications developed among the patients who remained quiescent in bed for ten to fourteen days after operation. Many who were equally poor as operative risks were permitted to get up on the first day, walk a few steps and sit in a chair with their legs elevated without mishap.

Pulmonary Complications.—Bronchopneumonia occurred only one third as often among the patients who were out of bed and walking within twenty-four hours. It is unlikely that this lowered incidence of pulmonary infection was due to modern chemotherapeutic agents and antibiotics, for these drugs were not used prophylactically. Massive atelectasis was not observed among the promptly ambulatory patients. The frequency of clinically recognizable partial atelectasis was unaffected. The incidence of pulmonary infarction due to small emboli, either demonstrable or suspected, was not influenced by prompt mobilization. However, massive pulmonary embolism of sufficient magnitude to cause a fatal catastrophe did not occur among the patients who were allowed to get up on the first postoperative day and increase their activity rapidly thereafter.

Vascular Complications.—Thrombosis in the deep veins of the legs was not prevented, nor was the incidence of this complication lowered by prompt postoperative mobilization. In these two groups thrombosis was actually commoner among the ambulatory patients. After studying the incidence of thromboembolism among 1,519 major surgical patients operated on at the Bassett Hospital and reported in 1947 [1] I concluded: "Exercises in bed, ambulation within the first twenty-four hours . . . and a generally accelerated convalescence permit an early return to customary activity. Unfortunately they do not favorably influence the incidence of postoperative thrombosis nor eradicate the hazard of pulmonary embolism." The present study of the incidence of postoperative thrombosis and nonfatal embolism after hernioplasty offers additional support to the same conclusions. This opinion is contrary to that held by many authors.

Gastrointestinal Complications.—Postoperative dilatation of the stomach and persistent abdominal distention were very much less common after hernioplasty when patients were permitted ambulation within the first twenty-four hours and prompt resumption of a normal diet. These complications occurred only six times among the 217 ambulatory patients but twenty-two times among the 157 patients in the late group.

Genitourinary Complications.—The total number of patients in the two groups who required catheterization once because of postoperative inhibition of the bladder was not significantly different. However, the necessity for repeated catheterizations was much less frequent after patients were up and about on their feet.

Fever of Unknown Origin.—Such fever was commoner among the patients who were recumbent during convalescence. The reason is not apparent.

Total Complications.—The incidence of total complications among the patients who were permitted prompt ambulation was 53 per cent, 1 complication after every other operation; among those who remained in bed for an average of eleven days the incidence was 98 per cent, 1 complication after every operation. The favorable influence of prompt ambulation on the incidence of total postoperative complications is obvious.

RECURRENCE AFTER HERNIOPLASTY

In studying recurrence after hernioplasty it is important to allow a follow-up interval of at least one year.[2] Consequently, all the hernias repaired in 1948 have been excluded from this phase of the survey.

1. Powers, J. H.: Postoperative Thromboembolism, Am. J. Med. **3**:224-230, 1947.

2. Glenn, F.: The Surgical Treatment of Five Hundred Herniae, Ann. Surg. **104**:1024-1029, 1936.

During the fifteen years from 1933 through 1947, there were 444 hernioplasties performed on 391 patients (table 4). Prompt postoperative activity was permitted after 193 of these procedures, early activity after 19 and late ambulation after 166; the remaining 66 hernioplasties were in children.

Fifteen hernias in the late group were immediately eliminated from further study by the death of 13 patients in the hospital. There were no recurrences among the 19 patients in the early group, nor were there any among the children. However, these two groups have been discarded because the former is too small to be of statistical importance and recurrence in infancy and childhood is exceedingly rare. Also eliminated because of death after discharge from the hospital without examination at least one year later or failure to trace for

TABLE 4.—*Rate of Recurrence Following Hernioplasty*

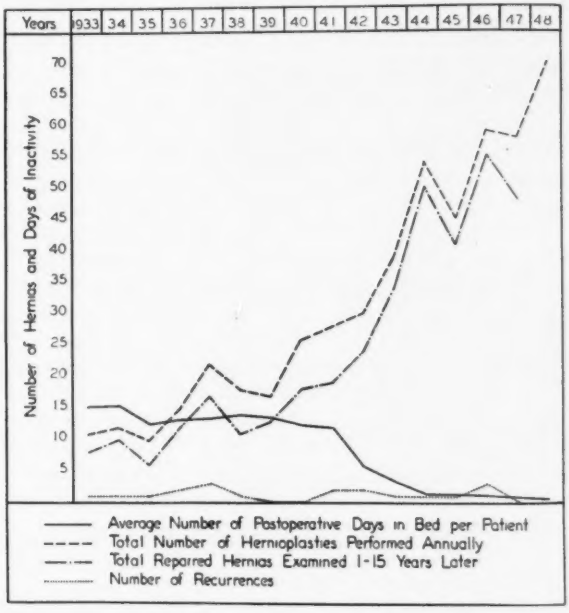
Analysis 1933-1947 Inclusive	Hernias Repaired				
	Adults Postoperative Activity			Children	Total
	Prompt	Early	Late		
Number of hernias repaired	193	19	166	66	444
Eliminated from further study by postoperative death of patient	0	0	15	0	15
Lost by death after discharge without follow-up examination	2	..	6	..	..
Discarded because of failure to trace for at least 1 year	11	..	16	..	..
Adequately followed for 1 to 15 years	180	11	129	47	367
Duration of follow-up period	1-8 yr.	..	1-15 yr.	..	..
Known recurrences	6	0	13*	0	19
Percentage of hernias adequately followed	3.3	..	10.1	..	5.1

* Only 2 of these recurred between eight and fifteen years after operation.

the same length of time were 13 hernioplasties among the promptly ambulatory patients and 22 among those in the late group. Finally remaining, adequately followed, reexamined and available for evaluation of the influence of prompt postoperative activity on the rate of recurrence were a total of 309 hernioplasties, 180 performed on patients who were promptly ambulatory after operation to be compared with 129 hernioplasties on patients whose mobilization was delayed for eleven days (table 4).

Prompt postoperative ambulation was instituted in 1941. Consequently, it was possible to reexamine the operative wounds in this group one to eight years after operation. The patients in the late group were followed for one to fifteen years. Six recurrences were discovered among the former and 13 among the latter, thereby establishing an absolute known rate of recurrence of 3.3 per cent among the patients who were allowed to get up and walk within twenty-four hours after operation and 10.1 per cent among those who remained recumbent in bed for eleven days. The known rate of recurrence for the entire group of 367 adequately followed hernias was 5.1 per cent.

The correlation of postoperative activity with rate of recurrence after hernioplasty is expressed graphically in the chart. In spite of the tremendous increase in the number of hernias operated on annually at the Mary Imogene Bassett Hospital during the past fifteen years and the striking decrease in the average length of time spent in bed by each patient after operation, the number of recurrences has remained essentially unchanged over the years. The annual rate of known recurrence has fallen steadily.



Graphic correlation of postoperative activity with incidence of recurrence following hernioplasty.

COMMENT

Prompt postoperative ambulation has no unfavorable effect on the clinical course of patients during convalescence from hernioplasties of all types. Mean temperatures and pulse rates rise no higher and actually return to normal levels more promptly.[3] Local pain and discomfort are inconsequential. The average length of hospitalization may

3. Powers, J. H.: The Abuse of Rest as a Therapeutic Measure in Surgery: Early Postoperative Activity and Rehabilitation, J. A. M. A. **125**:1079-1083 (Aug. 19) 1944.

safely be reduced to one week or less, and the long period of convalescence which formerly followed in the wake of surgical repair may be largely eliminated.[4]

SUMMARY

After 217 hernioplasties on 210 patients who were permitted to stand, walk and sit in a chair within twenty-four hours of operation there were 115 postoperative complications—an incidence of 53 per cent. After 157 operations on 153 patients who remained in bed for an average period of 10.8 days there were 153 complications—an incidence of 98 per cent.

Of 193 hernias repaired for 161 patients who were allowed prompt postoperative ambulation it was possible to reexamine 180 from one to eight years later; there were 6 recurrent hernias—a known rate of recurrence of 3.3 per cent. One hundred twenty-nine hernial repairs from a total of 166 hernioplasties on 152 patients who remained recumbent in bed for eleven days after operation were reexamined one to fifteen years later; there were 13 recurrences, a known rate of recurrence of 10.1 per cent (table 5).

TABLE 5.—*Incidence of Postoperative Complications and Rate of Recurrence Following Hernioplasty*

	Number				
	Postoperative Activity				
Summary Mary Imogene Bassett Hospital	Prompt	Early	Late	Children	Total
Complications 1933-1948					
Number of patients operated on	210	22	153	69	454
Number of operations	217	22	157	71	467
Deaths in hospital	0	0	15	0	15
Operative mortality (percentage)	0	0	10	0	3
Postoperative complications (number)	115	19	153	13	300
Incidence of complications per 100 operations	53	86	98	18	64
Recurrences 1933-1947					
Number of patients operated on	161	17	152	61	391
Number of hernias repaired	193	19	166	66	444
Number adequately followed (1 to 15 years)	180	11	129	47	367
Known recurrences	6	0	13	0	19
Rate of known recurrence (percentage)	3.3	0	10.1	0	5

CONCLUSIONS

Many postoperative complications are favorably influenced by prompt ambulation after hernioplasty. The incidence of venous thrombosis in the lower extremities and of pulmonary infarction due to small nonfatal emboli is unaltered.

The rate of recurrence following hernioplasties of all types is significantly less among promptly ambulatory patients.

4. Powers, J. H.: Evaluation of Early Postoperative Activity, Bull. New York Acad. Med. **22**:38-51, 1946.

PREVENTION AND MANAGEMENT OF THROMBOEMBOLISM

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THIS report is concerned with our experience in the management of thrombosis and embolism during the past nine years at the University of Michigan Hospital. In general, our methods are not new, but through diligent and everchanging application of preventive measures, to a great extent originally described elsewhere, we are able to report marked improvement in the incidence of the grave complications which are inextricably a part of thromboembolism. It is hoped that our experience may be of help to others similarly confronted with choosing between, and in many instances employing the combined effects of, the various methods of prevention and treatment.

The incidence of pulmonary embolism has been reported to be from 1 to 12 per cent in routine autopsies in various locations and with varying types and ages of patients.[1] Indeed, when the entire problem is considered and those patients found to have venous thrombosis are included with those in whom embolism was the first demonstrable sign, a most conservative estimate finds evidence of thromboembolic disease in 10 per cent of necropsies.[2]

It is now rather generally felt that slowing of the venous blood stream, injury to the intima of veins and certain changes in the composition of the blood are most important in the development of venous thrombosis. A host of other factors known to be important, such as age, obesity, nature of the primary disease or injury, type of operation and even weather, may be considered as exerting their influence in one or more of these categories, but the exact relationship is certainly not

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

From the Departments of Surgery and Internal Medicine, University of Michigan Medical School.

1. Belt, T. H.: Thrombosis and Pulmonary Embolism, Am. J. Path. **10**:129, 1934. Breslich, P. J.: Pulmonary Embolism, Journal-Lancet **58**:445, 1938.

2. McCartney, J. S.: Postoperative Pulmonary Embolism, Surgery **17**:207, 1945.

completely understood.[3] In general, it appears that operations of greater duration and magnitude, especially if intra-abdominal, and particularly if in the pelvis, are accompanied with the highest incidence of thrombosis and embolism.[4]

The maintenance of normal physiologic processes in periods of stress, following injury or postoperatively is a goal not easily attained by the application of a few simple measures. It is imperative to avoid all measures which contribute to the impediment of normal venous return. Position of the patient in bed so that venous blood pools in the pelvis and use of pillows under the knees, as commonly employed in Fowler's position, have been condemned previously.[5] Similarly, the advantage of the Trendelenburg position immediately after operation has been extensively discussed.[6] Patients with cardiac disease, in particular those with diminished cardiac output, can be restored to more nearly normal venous return with propitious restriction of salt and use of diuretics and digitalis, with reduction of risk of thromboembolism.[7]

For the patient in whom venous varicosities are apparent and immobilization contemplated, the simple expedient of applying elastic compression bandages has been found to be most useful in promoting better venous return by diverting venous blood from the superficial pools through the deeper venous pathways. Friedlander [8] advocated use of such bandages as early as 1935. We have not found the routine use of this method to be a practical measure, and the improper application of elastic bandages without frequent readjusting is worthless.

The major role of early ambulation on the improvement of the mortality rate from thromboembolism is now clearly apparent and is well reviewed elsewhere.[9] The more effective treatment of abdominal

3. Ochsner, A., and DeBakey, M.: Therapy of Phlebothrombosis and Thrombophlebitis, Arch. Surg. **40**:268 (Feb.) 1940.

4. Barker, N. W.; Nygaard, K. K.; Walters, W., and Priestley, J. T.: A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism, Proc. Staff Meet., Mayo Clin. **15**:769, 1940.

5. de Takats, G., and Jesser, J. H.: Pulmonary Embolism: Suggestions for Its Diagnosis, Prevention and Management, J. A. M. A. **114**:1415 (April 13) 1940.

6. de Courcy, J. L.: Venous Stasis as Cause of Postoperative Embolism: Its Prevention by Use of Reverse Fowler Position after Lower Abdominal Operations, Anesth. & Analg. **8**:342, 1929.

7. Ochsner, A., and DeBakey, M.: Therapeutic Considerations of Thrombophlebitis and Phlebothrombosis, New England J. Med. **225**:207, 1941. Gilbert, N. C.; de Takats, G., and Trump, R. A.: Effect of Digitalis on the Clotting Mechanism, J. A. M. A. **124**:736 (March 11) 1944.

8. Cited by Ochsner, A.: Intravenous Clotting, Surgery **17**:250, 1945.

9. Smith, L. A., and Allen, E. V.: Vascular Clinics: Studies of the Rate of Venous Blood Flow: Physiologic Studies and Relation to Postoperative Venous Thrombosis and Pulmonary Embolism, Proc. Staff Meet., Mayo Clin. **16**:53, 1941.

distention by means of continuous intestinal suction,[10] the wider application of the endotracheal tube in anesthesia, thereby extending adequate respiratory exchange to a greater number of patients, along with the encouragement of deep breathing exercises postoperatively[11] have all served to promote a more nearly normal flow of returning venous blood. The use of less painful transverse abdominal incisions has permitted earlier nonpainful deep respiration[12] and the actual insistence on exercise while the patient is in bed has undoubtedly been similarly helpful, although we have not seen fit to employ vigorous postoperative activity as recommended by Zava.[8]

If one is to accept Aschoff's[13] explanation of the origin of the venous thrombus and the view of Frykholm[14] and others that the thrombus is propagated in the venous stream from this original point of endothelial change, then it becomes most important to minimize damage to the venous intima by exerting great care when operating in the region of venous pathways. In a previous communication emphasis was placed on avoidance of performing venipuncture in veins of the leg.[15]

The major cause of death in fractures about the hip has been reported to be pulmonary embolism,[16] and prophylactic ligation following this injury has been advised for this reason.[17] Intimal injury to the large veins at the time of fracture, in addition to the slowing of the venous stream by edema, extravasation and immobilization, appears to be the predisposing factor in injuries of this region.

In severe crushing injuries, extensive operative procedures and also in widespread carcinoma undoubtedly many factors contribute to the

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10. Bellis, C. T., and Wangensteen, O. H.: Venous Circulatory Changes in Abdomen and Lower Extremities Attending Intestinal Distention, Proc. Soc. Exper. Biol. & Med. **41**:490, 1939.

11. Patey, D. H.: The Effect of Abdominal Operations on the Mechanism of Respiration, with Special Reference to Pulmonary Embolism and Massive Collapse of the Lungs, Brit. J. Surg. **17**:187, 1930; Artificially Induced Thrombophlebitis with Suggested New Approach to Problem of Postoperative Pulmonary Embolism, Surg., Gynec. & Obst. **64**:1002, 1937.

12. Coller, F. A., and Maclean, K. F., in Tribute to Lloyd Noland by Employees Hospital Reunion Committee, 1947.

13. Aschoff, L.: Thrombosis: Lectures in Pathology, New York, Paul B. Hoeber, 1924.

14. Frykholm, R.: The Pathogenesis and Mechanical Prophylaxis of Venous Thrombosis, Surg., Gynec. & Obst. **71**:307, 1940.

15. Lillie, R. H.: Pulmonary Embolism, Univ. Hosp. Bull., Ann Arbor **10**:93, 1943.

16. Golodner, H.; Morse, L. T., and August, A.: Pulmonary Embolism in Fractures of the Hip, Surgery **18**:418, 1945.

17. Allen, A. W.; Linton, R. R., and Donaldson, G. A.: Venous Thrombosis and Pulmonary Embolism: Further Experience with Thrombectomy and Femoral Vein Interruption, J. A. M. A. **128**:397 (June 9) 1945.

increased incidence of thromboembolism, possibly through the liberation of large amounts of thrombokinase.[18] Other changes in the blood reflected in the varying response to the administration of heparin sodium [19] and to variation in prothrombin concentration [20] have been correlated with the development of venous thrombosis and as a result have been suggested as possible prognostic tests for impending or early thromboembolism. We have not found any of these measures to be sufficiently practical for general clinical use.

Coincident with the widespread acceptance of many of the precautionary measures just mentioned have come reports of an unchanged incidence of venous thrombosis and pulmonary embolism.[21]

It has been most difficult to estimate the frequency with which venous thrombosis has occurred among our patients for several reasons. No doubt our acuity in making and willingness to make this diagnosis have increased rapidly in the past nine years as we have become more aware of the significance of thromboembolic disease. In similar manner it is felt that the pathologists have increased their ability to find an offending thrombus by examination of the veins of the lower extremities at autopsy. A third factor influencing the statistics on the frequency of venous thrombosis has been the insistence on the early application of preventive ligation and anticoagulant therapy, which has necessarily made it impossible to confirm the presence of venous thrombosis as the process was not allowed to reach its fully developed stage.

It has been encouraging to note the decline in the total incidence of pulmonary embolism among our patients as illustrated in chart 1. Since our active program of prevention began with venous ligation in cases of suspected or well developed venous thrombosis in the latter months of 1943, it is of interest that comparison of the incidence of pulmonary embolism for the last four year period shows a decrease from 169 to 53 cases (emboli being 31 per cent as frequent) when compared with a four year control period (chart 2), when only general measures were employed in the treatment of venous thrombosis. Among the patients with pulmonary embolism in the two four year periods, the mortality rate has not appreciably changed, being 38 per cent in the first four years and 42 per cent in the last four years.

Of great concern has been our apparent failure to improve the chances that the patient with cardiac disease will avoid thromboembo-

18. de Takats, G., and Fowler, E. F.: The Problem of Thrombo-Embolism, Surgery **17**:153, 1945.

19. de Takats, G., and Fowler, E. F.: Heparin Tolerance, Surg., Gynec. & Obst. **77**:31, 1943.

20. Sandrock, R. S., and Mahoney, E. B.: Prothrombin Activity, Ann. Surg. **128**:521, 1948.

21. Roe, B. B.: To be published.

lism. Although many more pulmonary emboli occur among surgical patients (222 in the eight year period 1940 to 1947 compared with 71 among medical patients), it is interesting to correct these figures for hospital admissions. During this period 24,637 patients were admitted to the medical wards and 75,031 to the surgical wards. The incidence

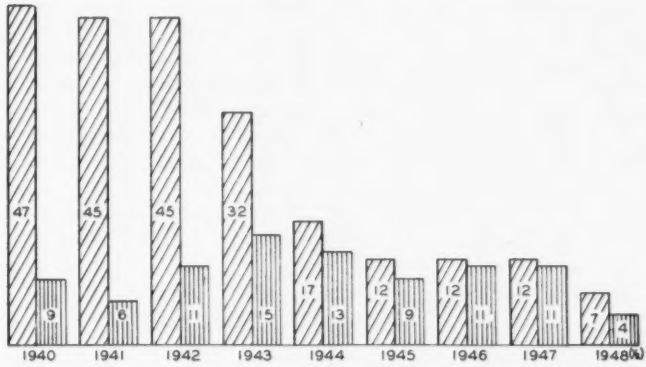

Chart 1.—Incidence of pulmonary embolism at the University of Michigan Hospital. The column at the left for each year indicates the number of patients without cardiac disease; that at the right, the number with cardiac disease.

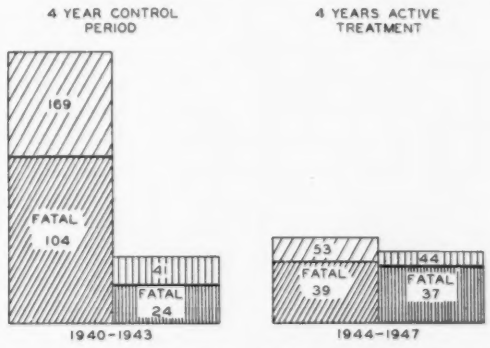

Chart 2.—Comparative incidence of pulmonary embolism. The column at the left for each period indicates the number of patients without cardiac disease; that at the right, the number with cardiac disease.

of pulmonary embolism is thus 2.96 per thousand among surgical admissions and 2.88 per thousand among nonsurgical admissions.

In reviewing the incidence of pulmonary embolism grouped according to the patient's primary disease, one finds the greatest number of

emboli occurring among the general surgical patients (chart 3). However, if one includes the patients with cardiac disease and corrects the incidence for numbers of patients admitted to each service, then the incidence is noticeably changed and it is the medical and, more particularly, the patient with cardiac disease who appears most vulnerable

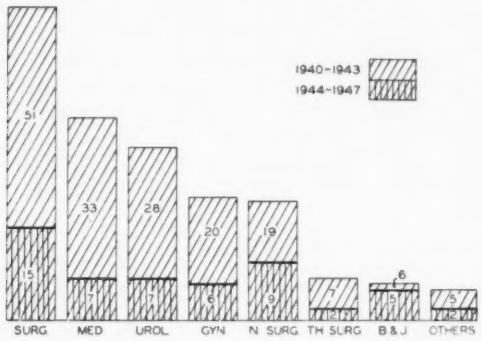

Chart 3.—Incidence of pulmonary embolism by service among patients without cardiac disease.

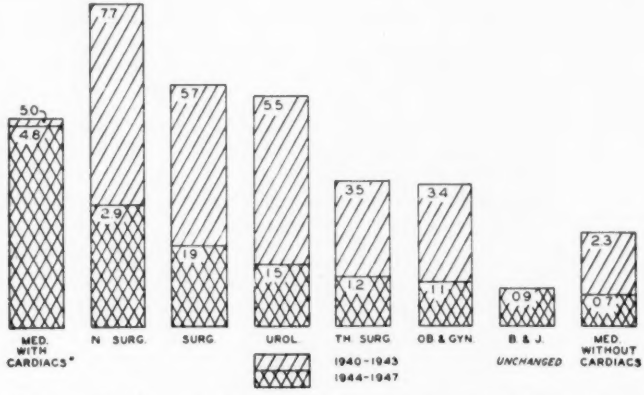

Chart 4.—Incidence of pulmonary embolism per thousand patients admitted to the hospital.

(chart 4). It is of interest that the medical patients without cardiac disease have demonstrated a sharp fall in thromboembolic disease similar to the improvement seen throughout the hospital. Again, it is obvious that little has been done for the patient with cardiac disease in reducing the incidence of venous thrombosis and embolism.

Since prevention of femoral-iliac-caval thrombosis has not been totally accomplished by the widely used general precautionary measures now employed, one must accept the possibility that further reduction in incidence of this disease may occur only after the protective use of venous ligation or the preventive use of anticoagulants. The use of either method alone or in combination on every patient admitted to the hospital as a means of prophylaxis seems hazardous and ill advised. On the other hand, to choose only those patients with specific diseases or those about to be subjected to specifically designated operations may be undesirable in many instances. In addition, the methods advocated and used successfully by some physicians may not be suitable to facilities available to others. Prophylactic measures must then be simple, readily available and effective. They must not affect adversely the primary disease; they must not be allowed to interfere with or complicate the desired treatment essential for the primary disease, and the morbidity and mortality associated with this prophylactic measure must be minimal.[22]

ANTICOAGULANTS

Heparin sodium has been employed in thrombosis, in embolism and after myocardial infarction when an immediate anticoagulant effect has appeared desirable. Usually the drug was continued until the prothrombin concentration had been substantially reduced (30 per cent or lower) by dicumarol,® the initial dose of which was given coincident with the first dose of heparin. The danger of thromboembolism in this "critical" period, following the initiation of dicumarol® therapy, is not easily estimated. In our experience, thromboembolism, progressive thrombosis or a repeated pulmonary embolus has appeared in a few instances prior to the obtaining of effective prothrombin levels with dicumarol.® This has led us to favor the more frequent use of heparin initially.

Heparin sodium has been administered intravenously either by continuous infusion [23] (100 to 200 mg. in 1,000 cc. of 5 per cent dextrose solution) or intermittently [24] (50 to 100 mg. at four to six hour intervals). In addition, a group of patients received intermittent intramuscular injections of heparin sodium.[25] If the drug is given by continuous infusion, care must be observed to control the flow at a uniform rate. The intermittent treatment, although more expensive and difficult

22. Coller, F. A.: Thrombo-Embolism, editorial, Surgery **17**:315, 1945.

23. Murray, D. W. G., and Best, C. H.: Heparin and Thrombosis: Present Situation, J. A. M. A. **110**:118 (Jan. 8) 1938.

24. Crafoord, C., and Jorpes, E.: Heparin as a Prophylactic Against Thrombosis, J. A. M. A. **116**:2831 (June 28) 1941.

25. Walker, J.: The Efficacy of Heparin Administered by Intravenous, Intramuscular and Subcutaneous Routes, Surgery **17**:54, 1945.

to carry out over a prolonged period, is preferable for a patient in whom a continuous thirty-six to forty-eight hour infusion may be impractical.

Although, to some extent, the dosage requirements of heparin are related to body weight, they can be estimated only by the frequent determinations of the blood-clotting time. For this purpose, we have used the Lee and White test by which values up to eleven minutes are normal. Though we have no proof that control of a thromboembolic process is necessarily favored when the dosage of heparin is regulated by clotting tests, performance of such tests prior to the start of treatment and at least once daily thereafter is recommended as a safeguard against excessive prolongation of the clotting time. An adequate heparin effect has been obtained, in our opinion, when the clotting time has been doubled (fifteen to twenty-five minutes). Since heparin produces enormous prolongation of the prothrombin time, care must be observed to obtain blood for determinations of prothrombin time (in estimating the dosage of dicumarol®) three to four hours after the last dose of heparin. Heparin does not generally appear to hasten the reduction of prothrombin by dicumarol.® As prothrombin activity is reduced by dicumarol,® however, increased sensitivity to heparin may be anticipated.

Heparin sodium occasionally induces a mild foreign protein reaction or it may produce hematuria and wound hemorrhage. The incidence of these complications is considerably less than that of the complications associated with dicumarol.® Since the effect of heparin is limited to a three to four hour period, minor cases of bleeding may be expected to cease spontaneously. Intravenous injection of protamine sulfate may also be employed quickly to reverse the effect of heparin, and blood transfusion is indicated in the event of severe bleeding. Vitamin K is of no value to reverse the effect of heparin.

Dicumarol® must be given orally and is available in 50 and 100 mg. capsules. Soon after ingestion it is rapidly removed from the stomach or upper gastrointestinal tract. Reduction of the prothrombin content of peripheral blood is the only known physiologic effect of dicumarol.®

Adequate facilities for measuring prothrombin are essential for the safe and effective administration of dicumarol.® The Quick procedure has proved eminently successful for this purpose. By the unmodified Quick test, employing whole plasma and potent thromboplastin (of which there are several reliable commercial sources), the normal prothrombin time is remarkably constant, varying from twelve to sixteen seconds (assumed to represent 100 per cent prothrombin concentration). Prothrombin activity may be expressed in terms of seconds of "prothrombin time," or as percentage of prothrombin (calculated from the formula $\frac{\text{normal prothrombin time [seconds]}}{\text{patient's prothrombin time [seconds]}} \times 100$) or, after interpolation from a prothrombin dilution curve, as "percentage of normal prothrombin concentration."

We have preferred to express prothrombin activity in terms of percentage of normal concentration. By this method the effective range of concentration, through practical experience, has been found to be less than 30 per cent and greater than 10 per cent. It is evident that thromboembolism is less common at concentrations below 30 per cent. Utilization of this expression of prothrombin activity implies the construction of frequent dilution curves, which, for the small laboratory, is difficult if not impossible. In these circumstances it is agreed that the preferable expression of prothrombin activity is in seconds of "prothrombin time." The clinician must always be informed of the prothrombin time of the control (normal) plasma as well as that of his patient. Reasonable daily consistency of the control value (variation not in excess of four seconds) is imperative and is the key to the safe administration of dicumarol.® When this is assured, the drug may be given to prolong the patient's prothrombin time to values twice the control but not in excess of thirty-five seconds. Such values, for practical purposes, compare favorably with the effective range of prothrombin concentration (10 to 30 per cent).

Dicumarol® is usually given initially as a single 300 mg. dose, following a pretreatment determination of prothrombin concentration. Thereafter, the dosage must always be estimated on the basis of daily prothrombin determination. When this is expressed in terms of percentage prothrombin concentration, from 100 to 200 mg. of the drug, dependent on the patient's response, is given each day that the concentration is 20 per cent or above; the drug is withheld when the concentration is below 20 per cent.

In our experience prothrombin concentration will be reduced by dicumarol® to the therapeutic range in an average of 2.8 days. The initial effective dosage of dicumarol® proved to be about 600 mg.; approximately 900 mg. was administered in the first week of treatment, and the average total dose (to obtain about ten days of effective prothrombin levels) was 1,400 mg. Six days after the last dose of dicumarol® the prothrombin was usually found to be elevated to the normal range (70 to 100 per cent prothrombin concentration).

There is considerable variation in sensitivity to dicumarol® not reflected by these figures. The time required to obtain an effective level was not materially lessened unless the pretreatment prothrombin level was in the range of 50 per cent concentration or below, when an effective level was obtained in about 1.7 days. About 10 per cent of our patients with normal pretreatment prothrombin levels were reduced to 30 per cent prothrombin concentration within twenty-four hours by a single 300 mg. dose of dicumarol.® By way of contrast, in about the same percentage of cases from 1,000 to 1,800 mg. of dicumarol® was required before the effective range was reached.

We have observed increased sensitivity to dicumarol® in patients with major hepatic or renal insufficiency; in some patients with cardiac failure, and on two occasions in patients with severe acidosis and alkalosis. In occasional patients dicumarol® induces nausea, vomiting and abdominal cramps. Low prothrombin levels may be associated with a distinct feeling of malaise and fatigue.

Effective levels of prothrombin were maintained about 6.5 days in the average postoperative patient to whom dicumarol® was given prophylactically; treatment was usually instituted on the first or second postoperative day. About ten days of effective prothrombin concentration levels were maintained in patients with peripheral venous thrombosis. Similar concentrations for two weeks are advised in patients

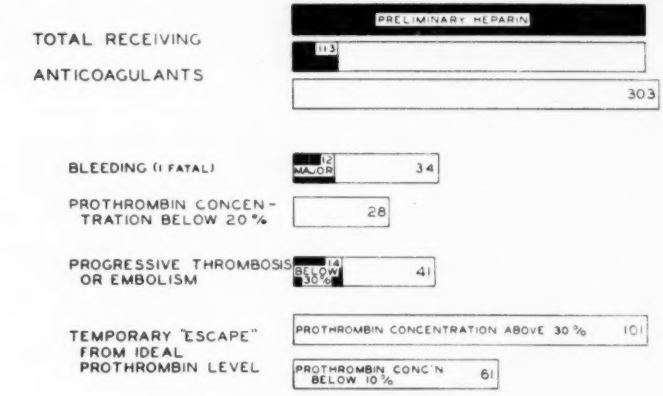

Chart 5.—Complications of anticoagulant therapy.

with pulmonary infarction and from three to four weeks in patients with myocardial infarctions.

Perfect control of prothrombin concentration in the effective range should not be expected with dicumarol.® In our experience with 303 patients (chart 5), temporary and accidental escape of prothrombin above the 30 per cent concentration occurred at some time in 101 (33 per cent) of the cases. An average of 300 mg. of the drug was required to correct such a rise. In a few cases, in these circumstances, thromboembolism may be expected to progress.

Temporary decline of prothrombin levels to less than 10 per cent concentrations occurred in 61 (17 per cent) of the patients after an average of 850 mg. of dicumarol® and persisted for an average of 1.5 days. The fact that in less than 10.5 per cent of these patients there was bleeding emphasizes that hypoprothrombinemia of this magnitude

need not be viewed with alarm. If spontaneous correction has not occurred within twenty-four hours, vitamin K should be administered, a single intravenous injection (72 mg. of menadione sodium bisulfite) being usually sufficient.

Every physician administering dicumarol® should realize that reduction of prothrombin to effective levels is associated with a definite incidence of bleeding, averaging 11 per cent in our experience. The prophylactic use of the drug in postoperative patients is associated with an increase in the incidence (16 per cent) and severity (in 6 of 10 cases bleedings were major in extent) of this complication. In two thirds of the cases hemorrhage occurred at a prothrombin concentration of less than 20 per cent and in one fifth in the range below 10 per cent. The severity of bleeding is not necessarily related to the prothrombin level at which it occurs, and patients should not be discharged from the hospital until the prothrombin concentration is above 50 per cent.

The physician responsible for the administration of dicumarol® should be prepared in the event of severe or persistent hypoprothrombinemia and severe or persistent bleeding to reverse its effect by large doses of vitamin K. We recommend in the event of excessive bleeding that 72 mg. of vitamin K (menadione sodium bisulfite) be given intravenously every four hours for four to six doses or until the bleeding ceases. In the average case of minor bleeding, in our experience, an average of 185 mg. of vitamin K was required; in cases of major bleeding an average of 272 mg. was required before bleeding ceased. Such large doses have not been associated with toxic effects. In the event of severe hemorrhage, blood transfusions should be freely used to supplement vitamin K.

From our experience with the 1,150 patients who form the background of the study, the following indications for the use of the chemical anticoagulants as active prophylactic measures may be outlined.

Prophylactic Anticoagulant Therapy (No Venous Thrombosis)

1. Recent episode of thromboembolism; immobilization contemplated
2. Severe contusions of the lower limbs
3. Obesity; immobilization contemplated
4. Retroperitoneal tumor
5. Operation in the region of major vessels
6. Arterial embolism
7. Transverse myelitis
8. Pelvic inflammation
9. Varicose veins, untreated
10. Congestive heart failure; myocardial infarction

It is difficult to define the "safe" period for a given patient when freedom from pulmonary embolic episodes may be expected following

venous thrombosis. Treatment of every patient with a suspected history of venous thrombosis within his lifetime would be unfeasible. However, one can say that any patient who has had a previous episode of thrombosis or embolism within the past year and is facing operation or prolonged rest in bed should not be denied active preventive measures. For those patients who have had a manifestation of thromboembolism many years previously, the general preventive measures described earlier should be assiduously applied and early treatment carried out if thrombosis or embolism appears.

Direct trauma to blood vessels is an obvious cause of intravascular clotting. In other instances propagation of the thrombus from the site of injury into the major veins of the extremity may occur. The increase in formed elements of the blood and its increased coagulability as a result of tissue damage also favor the production of a thrombus. An ideal set of circumstances then exists when, in addition to these factors, the part is immobilized in a plaster cast or in a complicated traction apparatus. That intravenous clotting does not always occur in such instances is not easily explained.

The role of obesity as a factor predisposing to thrombosis is difficult indeed to evaluate.[26] Certainly the loss or diminution in the vascular tone of obese patients may accentuate slowing of the blood stream when inactivation is necessary. Many of these persons have a considerably reduced range of pulmonary excursion in the supine position. It seems more than coincidence that a vast number of patients in whom intravascular clotting occurs are obese. For an extremely obese person, when an extensive operative procedure and immobilization are planned prophylactic use of anticoagulants might well be considered.

A large number of the tumors occurring in or extending to the retroperitoneal area will result in progressive venous obstruction. Increasing weakness, lethargy and inactivity may aid in the deposition of a soft thrombus in the extremities of such patients. Before the tumor completely occludes the major venous channels, a massive pulmonary embolus resulting in the death of the patient may intervene. When reasonable palliation or curative therapy is contemplated for such tumors, measures to prevent this accident should be carried out. Venous ligation is usually technically unfeasible in such patients.

Operations such as inguinal and iliac lymphadenectomy, combined abdominoperineal resection and urinary cystectomy which are performed in the immediate vicinity of great vessels are also often instances of direct trauma that result in the intimal damage responsible for the inception of a venous thrombus. The injury to soft tissues resulting from these and other more or less extensive operations and the changes

26. Snell, A. N.: Relation of Obesity to Fatal Pulmonary Embolism, Arch. Surg. **15**:237, 1927.

occurring in the blood constituents which appear in long and difficult procedures favor the progression of such a nidus.

The profound ischemia or inadequate dilatation of collateral arteries induced by the vasospasm after sudden arterial occlusion produces changes in the intima of both arteries and veins which if prolonged result in widespread thrombosis. Therefore, treatment of the patient with acute arterial occlusion should include not only the relief of vascular spasm and arterial obstruction by embolectomy when possible but also the prevention of extending venous thrombosis by the administration of anticoagulants. In arterial embolism, the lapse of time prior to relief of occlusion is of greatest importance from the standpoint of both viability of the part and extension of the thrombosis, and after embolectomy the administration of anticoagulants should be instituted.

Patients with complete transection of the spinal cord usually have loss of normal vasomotor responses and, as a result, a warm, dry extremity with maximal vasodilatation. Because of this fact, many observers have considered phlebothrombosis as an unlikely complication in this group of patients. Schneider [27] followed 58 such patients in a service-connected neurosurgical service and found the death of one patient due to a pulmonary embolus. Ten patients in the series under consideration exhibited evidence of thromboembolism following transverse myelitis. Six of these patients died with massive or multiple, recurring pulmonary emboli.

The use of anticoagulants in this type of patient should be withheld until the danger of continued bleeding into the traumatized spinal cord or from the site of surgical exploration is no longer present. In most instances, anticoagulants may be begun as early as forty-eight hours after injury or operation. Ligation of the inferior vena cava seems an acceptable alternative, provided it can be carried out early and without endangering the patient's recovery. Anticoagulant prophylaxis should be continued until the patient is no longer restricted to bed, which for a large number of patients will be approximately three months following injury. Those patients requiring longer immobilization should be offered the protection of ligation of the vena cava. In the face of complications necessitating immobilization of an already ambulatory patient, ligation of the vena cava or a repeated course of anticoagulants is suggested as the best protection against massive fatal pulmonary embolism.

Mechanical or infectious trauma to pelvic veins frequently occurs after pelvic laparotomy, in the postpartum period, after a difficult labor, instrumental delivery or cesarean section and in the presence of puerperal sepsis or other forms of widespread pelvic inflammatory disease. Often these patients are immobilized in bed for a long time, and pelvic

27. Schneider, R. C.: Personal communication to the authors.

trauma is a potential source for the development of an extending venous thrombosis. Allen, Barker and Hines [28] have cited an incidence of pulmonary embolus from 1.25 to 12.5 per cent after gynecologic operations.

Meisen [29] has stated that 10 to 17 per cent of the general population have varicose veins and after the age of 20 the incidence in women is approximately four times that in men. The development of varicosities in obese persons is considerably enhanced. In the large, saccular superficial veins pooling of blood readily occurs when the extremity is dependent or light pressure is exerted above the varix. Intimal sclerosis and inflammatory infiltration in the perivenous tissues are common histologic observations. Thus, stasis and intimal damage, two of the three commonly accepted prerequisites of intravascular clotting, are already present in these patients. Once clotting is initiated, extension through the communicating vessels into the major venous trunks is readily accomplished, although this is by no means the commonest manner in which femoral thrombosis is initiated.

Surgical extirpation of varicose veins is the only certain means of eliminating them as a source of future thrombosis. The application of compression bandages to the lower extremities to obliterate the superficial veins is often adequate but equally often is an unreliable means in our experience of accomplishing the same end. When definitive treatment, such as surgical extirpation, cannot be accomplished because of the urgency of the patient's disease, anticoagulant prophylaxis is a useful means of preventing thrombosis.

The incidence of thromboembolism as a complication of coronary thrombosis with myocardial infarction has been reported as varying from 37 per cent on the basis of clinical findings [30] to 45 per cent in autopsy cases.[31] By the prompt institution of anticoagulant therapy after a myocardial infarction, it is hoped that the formation of mural thrombi and subsequent embolic showers may be forestalled. The anticoagulants may serve to halt the extension of the initial coronary thrombosis by propagation as well as the formation of new thrombi in other coronary branches and to prevent the development of thromboses in the pelvic and leg veins, from which the majority of fatal pulmonary emboli have their origin.[32] The recently reported cooperative study of

28. Allen, E. V.; Barker, N. W., and Hines, E. A.: Peripheral Vascular Diseases, Philadelphia, W. B. Saunders Company, 1946, p. 592.

29. Meisen, V., cited by Allen, Barker and Hines,[28] p. 665.

30. Nay, R. M., and Barnes, A. K.: Incidence of Embolic or Thrombotic Processes During Immediate Convalescence from Acute Myocardial Infarction, Am. Heart J. **30**:65, 1945.

31. Hellerstein, H. K., and Martin, J. W.: Incidence of Thrombo-Embolic Lesions Accompanying Myocardial Infarction **33**:443, 1947.

32. Nichol, E. S.: Treatment of Acute Coronary Thrombosis with Dicumarol: Further Observations, Am. Heart J. **33**:722, 1947.

the American Heart Association [33] indicates that by the proper use of anticoagulant therapy the mortality rate of coronary thrombosis can be reduced from approximately 23 per cent (control series) to 13 per cent and the incidence of thromboembolic complications from approximately 19 per cent to 9 per cent. Our experience, in a small series of patients with myocardial infarctions, is in agreement with these figures. Although this form of treatment, as the figures indicate, is not completely protective, it is recommended that, for the most part, every patient with a myocardial infarction be given the benefit of anticoagulant therapy.

There is need to put into practice measures which will aid in reducing the frequency and gravity of thromboembolism as a complication of other forms of heart disease. Carlotti and co-workers,[34] in a study dealing with the problem of pulmonary embolism among medical patients at the Massachusetts General Hospital over a ten year period, reported that from 59 to 71 per cent of pulmonary embolisms occurred in patients with cardiac disease, especially the rheumatic, hypertensive and coronary forms. Auricular fibrillation was present in nearly one third, and congestive failure was frequently present. In patients with massive pulmonary embolism in whom the leg veins were examined at autopsy, 75 per cent showed thrombosis. Thrombi were found in the right side of the heart in relatively few. In cardiac failure the development of thromboembolism is favored by the increased viscosity of the blood associated with the hemoconcentration accompanying shock and by venous stasis concomitant with decrease in cardiac output.[35] Venous dilatation on the basis of obstruction, decrease in movement of the legs with enforced rest in bed and limitation of respiratory excursion further increase peripheral venous stagnation. Venous thrombi, in these circumstances, must be masked many times by peripheral edema.

White [35] has stressed that in a patient with cardiac disease with congestive failure who fails to respond as he should to treatment the commonest complication is pulmonary embolism and infarction, easily overlooked and often diagnosed incorrectly. In our experience with 15 such patients, it appeared that the majority had sustained at least one infarction before admission to the hospital. The fact that definitive treatment was not instituted in these patients for an additional period of five days following admission indicates the general lack of awareness of the frequency and gravity of pulmonary embolism in these patients.

33. Wright, I. S.; Marple, C. D., and Beck, D. F.: Anticoagulant Therapy of Coronary Thrombosis, J. A. M. A. **138**:1074 (Dec. 11) 1948.

34. Carlotti, J.; Hardy, I. B.; Linton, R. R., and White, P. D.: Pulmonary Embolism in Medical Patients, Am. Heart J. **33**:737, 1945.

35. White, P. D.: Heart Disease, ed. 3, New York, The Macmillan Company, 1947, p. 635.

Recognizing that much of the thromboembolism in cardiac and other serious diseases is terminal, it still appears likely that much might be done to reduce the gravity of the problem. Prophylactic interruption of the femoral vein has been recommended when pulmonary embolism is discovered in patients with cardiac disease.[34] Homans[36] stated: ". . . if, in any instance of heart disease in which confinement to bed for more than a week is expected, embolism is believed to have occurred (from thromboses clinically evident or presumed to be present in the lower limbs), both common femoral veins should be explored and ligated. When there are actual contraindications for the anticoagulants, such a rule may be counted imperative; otherwise it is a matter for professional experience and judgment to determine." Although patients in congestive failure sometimes prove unusually sensitive to dicumarol,[9] we prefer the more extensive use of prophylactic anticoagulant therapy to venous ligation in this group. We are aware, moreover, that the mortality rate is still considerable despite either course of action. In our experience, despite effective concentrations of prothrombin, death occurred in 33 per cent of the patients with cardiac disease complicated by congestive failure and pulmonary infarction. By comparison, the mortality rate was 28.3 per cent in a group of 60 patients treated by ligation in Carlotti's series, and in the control group of 213 patients treated without ligation the mortality rate was 50.7 per cent.

It is becoming evident that special indications for long range prophylactic anticoagulant therapy may exist in some patients with heart disease. Wright,[33] in particular, emphasized these benefits in the case of the patient with old rheumatic heart disease, auricular fibrillation and intracardiac thrombi from which showers of emboli have occurred.

Contraindications to Anticoagulants

1. Lack of adequate laboratory control
2. Extreme old age (variable)
3. Repeated infarction, progressive thrombosis or major hemorrhage during anticoagulant therapy
4. Recent cerebrovascular accident
5. Major renal or hepatic damage
6. Ulcerative or granulating lesions, potential source of extensive bleeding
7. Central nervous system lesions after operation or constituting special bleeding risk
8. Obstetric conditions in which bleeding is a major hazard
9. Blood dyscrasias with a bleeding tendency
10. Subacute bacterial endocarditis

36. Homans, J.: Operative Treatment of Venous Thrombosis in the Lower Limbs, Am. J. Med. **3**:345, 1947.

Several of the important contraindications to anticoagulant therapy are outlined in the preceding tabulation. The most important obstacle to the widespread use of dicumarol® is lack of satisfactory laboratory tests to measure prothrombin activity. It cannot be too greatly stressed that administration of the drug is almost by necessity limited to hospitalized patients and in the absence of reliable prothrombin tests is ill advised.

Patients with severe hypertension and known past cerebrovascular accidents are poor risks for anticoagulant therapy; fatalities in these circumstances have occurred in our experience. Anticoagulant therapy has been employed in some carefully selected cases of cerebral thrombosis. It is questionable whether the beneficial results of this form of treatment are significant or constant enough to justify the involved risks.

Dicumarol® is believed to reduce prothrombin activity through its effect on the liver, and both dicumarol® and heparin are presumably eliminated in part by the kidneys. Major impairment of renal and hepatic function definitely increases sensitivity to dicumarol®, and some patients with congestive failure are likewise sensitive, presumably on the basis of reduced renal blood flow. In these circumstances heparin and dicumarol® should be employed with caution.

Anticoagulant therapy is further contraindicated in patients with known but inaccessible ulcerative, granulating or bleeding lesions which constitute a potential source of extensive bleeding. Such lesions are commonly encountered in the gastrointestinal tract.

Recent surgical procedures on the eye or on the central nervous system or on its lesions constitute special contraindications to anticoagulants from the fact that a small amount of bleeding in these circumstances conceivably could produce irreversible damage. In a variety of special gynecologic and obstetric situations in which bleeding is a prominent feature the use of anticoagulants would be unwise. These drugs should be employed with caution in the last trimester of pregnancy.

Patients with blood dyscrasias, with a bleeding tendency, are poor risks for anticoagulant therapy. Subacute bacterial endocarditis, with its increased bleeding tendency, has generally come to be recognized as a contraindication to the use of heparin and dicumarol,® and an appreciable percentage of the deaths attributed in the literature to the latter drug have occurred in patients with subacute bacterial endocarditis.

VENOUS LIGATION

In discussing venous ligation it will be pointed out that patients facing an imminent operation and the very elderly person might best have their venous thrombosis treated with vein ligation to obviate hemorrhagic risks attending anticoagulant therapy.

Now that some of the enthusiasm for ligation of the femoral vein has abated, it is well to attempt to evaluate its place in the prevention and treatment of thromboembolism.

There are many physicians who feel that, because a fresh venous thrombus is only loosely attached to the vein wall, it is imperative that either thrombectomy or ligation of the vein above the thrombus be carried out at once whenever the diagnosis of phlebothrombosis is made. Ochsner [37] has expressed the belief that this procedure should take precedence over every other operative procedure except measures to combat massive hemorrhage.

The technic of ligation of the femoral and iliac veins and the inferior vena cava have been described in detail elsewhere.[38] Whenever ligation of a femoral vein was indicated and a thrombus was found extending into the common femoral vein, an attempt was made to ligate above the clot. Thus, ligations of the superficial femoral vein were done, for the most part, when no clot was detectable above this level. Thrombectomy was performed in all cases in which it was possible to demonstrate a clot. Ligations of the inferior vena cava have been carried out through a retroperitoneal approach, the vessel being ligated in continuity and above the clot.

When the major failures of vein ligation are reviewed (chart 6), however, some reconsideration of its widespread application is necessary. The primary reason for concern in patients with phlebothrombosis is the occurrence of pulmonary embolism; in 10 of our patients embolism occurred after ligation was carried out, an incidence of 6 per cent of failure of protection. More disturbing are the cases of the 3 patients in whom a fatal massive pulmonary embolus occurred in the postligation period. Two of these patients had only a unilateral femoral ligation, but in the third both superficial femoral veins were ligated. This is an object lesson indeed for those who feel that bilateral ligation offers complete protection from pulmonary embolism. Four patients on whom ligations were carried out had one or more subsequent embolic episodes which contributed to their deaths. Again, complete protection was anticipated in 1 of these when the inferior vena cava was ligated. In this patient recurring pulmonary emboli appeared after anticoagulant therapy, and he was critically ill at the time of subsequent caval ligation. The postligation embolus would undoubtedly have been nonfatal in a less debilitated person. In the 3 patients who had minor emboli after ligation, only unilateral ligations were done and it is sus-

37. Ochsner, A.: Venous Thrombosis, Surgery **24**:445, 1948.

38. Homans, J.: Exploration and Division of the Femoral and Iliac Veins in the Treatment of Thrombophlebitis of the Legs, New England J. Med. **224**:179, 1941. Northway, R. O., and Buxton, R. W.: Ligation of the Inferior Vena Cava, Surgery **18**:85, 1945.

pected that the subsequent emboli originated in the opposite leg. In 1 patient hemorrhage during ligation necessitated postponement of the ligation. Subsequently, this was accomplished without event.

Extreme postligation edema has been suggested as a serious complication by Dennis.[39] We have not seen it seriously endanger the extremity of a patient, but in 1 of our patients bilateral ligations were carried out on separate occasions and each ligation was followed by tremendous edema of the leg. It is interesting to note that the superficial femoral and greater saphenous veins were ligated on one side, while the common femoral and saphenous veins were ligated on the other.

Despite the obvious failure in a few instances of ligation of femoral or iliac veins or of the vena cava to protect against embolic accidents,

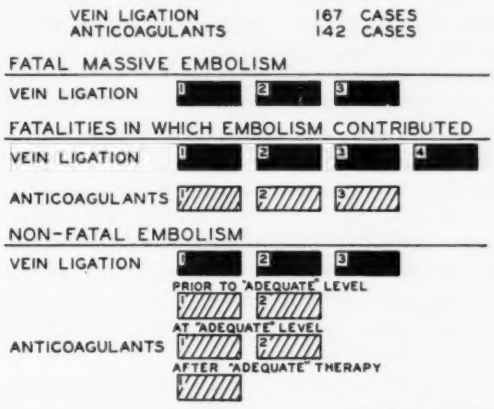

Chart 6.—Failure of prevention of pulmonary embolism in cases of venous thrombosis.

there is a definite need and place for this procedure in the treatment of phlebothrombosis. It must be emphasized, however, that ligation below the level of the inferior vena cava must be bilateral to be adequate. It seems likely that many of the cited evidences of failure were due not to the ineffectiveness of the method but to the fact that the ligations were unilateral.

The most obvious need for ligation lies in those instances in which the use of anticoagulants is contraindicated, regardless of whether the contraindication is technical in that laboratory facilities are unavailable or whether the contraindications are specifically medical, as in a patient who is bleeding.

39. Dennis, C.: Disaster Following Femoral Vein Ligation for Thrombophlebitis, Surgery **17**:264, 1945.

Venous ligation is often a necessary alternative in patients with septic thromboembolism. In such instances thrombosis in small vessels may be an important part of the defense mechanism of the body which prevents uninhibited extension of the suppurative process. In such instances the choice between ligation and anticoagulants will depend largely on the sensitivity response of the infecting organism to the antibiotic and chemotherapeutic agents.[40] If the organism should prove unresponsive to these agents, the anticoagulants would be undesirable and vein ligation could be effectively substituted. On the other hand, when the infecting organism responds readily to the available antibacterial agents or when the suppurating focus can be readily excised,[41] control of progressive thrombosis may be suitably carried out by anticoagulants.

In thrombosis of the saphenous vein proximal saphenous ligation accompanied with early ambulation seems to us to be the simplest effective treatment. Anticoagulant therapy in this instance may be hazardous and usually no more effective.

Absolute contraindication to ligation of either the superficial or the deep venous systems exists only when the desired ligation site is compromised by an extensive burn, infection or neoplasm.

The frequency of pulmonary complications following amputations of a leg was estimated by Veal to be 14.9 per cent in the 275 cases which he reviewed,[42] and he stated that many of these pulmonary lesions were embolic in origin. DeTakats, in his discussion of Veal's paper, noted that in 110 patients undergoing major amputations in his experience between 1927 and 1942 there was 1 who died of a pulmonary embolus following amputation.

At the University of Michigan Hospital 373 amputations of the leg were performed between 1939 and 1948 and 6 patients during this period had pulmonary emboli following amputation, an incidence of 1.6 per cent. Because of our concern for the risk of embolism in our patients on whom amputation has been carried out, prophylactic ligation of the femoral vein on the amputated side was carried out on 39 patients. The corrected incidence of pulmonary embolism on the 334 patients on whom amputations were carried out without ligation is thus 1.2 per cent, or four times the average for our surgical patients.

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40. Sandblom, P.; Ekström, G., and Quist, O.: Treatment of Local Pyogenic Infections with Heparin, Acta chir. Scandinav. **96**:323, 1948.

41. Neuhof, H., and Seley, G. P.: Acute Suppurative Phlebitis Complicated by Septicemia, Surgery **21**:831, 1947.

42. Veal, J. R.: Prevention of Pulmonary Complications Following Thigh Amputation by High Ligation of Femoral Vein, J. A. M. A. **121**:240 (Jan. 23) 1943.

Pulmonary embolism occurred after amputation in 4 patients without ligation and in an additional 2 patients after the femoral vein was tied. In neither of the last 2 patients did death result from the pulmonary embolus. Of interest is the fact that both fatal emboli occurring in the unligated group following amputation were accompanied with gas infection of the soft parts of the leg of such extent that ligation was felt inadvisable. Both of these cases occurred before the advent of anticoagulants or present day antibiotics. It is possible that the fatal outcome was assured by the severe toxicity associated with this type of infection.

It now appears that two reasons for failure of this operative procedure as a means of protecting the amputee from embolism are (1) an insufficiently high level of ligation and (2) failure to perform bilateral ligation. Most of the patients in this group were elderly arteriosclerotic patients, many with diabetes. Relief of pain is commonly obtained by these patients by allowing the leg to hang in a dependent position, and many of the patients are necessarily confined to bed for long periods preoperatively, all factors which tend to increase the incidence of thromboembolism.

Since ligation of the inferior vena cava is a hazardous prophylactic measure in these elderly patients, we feel that the incidence of pulmonary embolism can be greatly reduced by ligation of the common femoral vein on the side of amputation and additional ligation of the superficial femoral vein on the opposite side. These measures, carried out at the time of amputation, should offer the best protection to the patient against embolism and result in a minimum of postligation sequelae.

Since the prescribed indications for ligation or anticoagulant therapy often must be adjusted to meet the needs of the patient's disease, instances do exist for the substitution of one form of treatment for another or for their combined use.

Indications for Combined Therapy

1. Progressive thrombosis or embolism subsequent to one of treatment
2. Necessary interruption of anticoagulant therapy due to
   a. Hemorrhage
   b. Intercurrent surgery
   c. Intercurrent disease in which anticoagulants are undesirable

In chart 6 are listed the complications incident to one or the other form of treatment of thromboembolic disease. In several instances infarction occurred subsequent to the use of the indicated type of vein

ligation or adequate prolongation of the prothrombin time. Likewise, while adequate protection was given against new or repeated pulmonary emboli by venous ligation, progressive or recurrent thrombosis did occur occasionally in the blocked extremity. Such instances afford good reason for the substitution or addition of the other method of treatment. Along with such examples must be mentioned those patients in whom satisfactory progress is occurring with anticoagulant measures but in whom intercurrent operations become suddenly mandatory or a complicating disease becomes apparent toward which anticoagulants would be detrimental. An additional small number of patients in whom individual idiosyncrasies to the anticoagulant drugs are seen must be protected from the fatal sequelae of thromboembolism by venous ligation.

After consideration of the instances in which the use of anticoagulant therapy is ill advised, either in the active management of patients with thromboembolism or as a measure in the prevention of this disease, one must then define the instances for its choice as an effective therapeutic measure. We are of the opinion that the anticoagulants, heparin sodium and dicumarol,® are the best means of preventing venous thrombosis and subsequent pulmonary embolism in all patients in whom definite contraindications to their use, as described, do not exist. Similarly, once thromboembolism has occurred, either in the postoperative patient, during enforced rest in bed or immobilization, or in the patient on normal activity, these chemicals when used intelligently and judiciously again afford excellent protection to the patient.

Available for follow-up study more than six months after venous ligation were 99 patients in whom thromboembolism was suspected or apparent (chart 7). Of those having ligations of the common femoral vein 35 per cent had swelling of the entire leg on which the ligation was performed—designated as 3 plus swelling on the accompanying chart. In the same group 24 per cent had swelling of calf and ankle (2 plus) and in 18 per cent the ankle (1 plus) was the only site of swelling. Pain caused some complaint in 41 per cent.

Patients having ligations of the superficial femoral vein had less severe swelling; 19 per cent had 3 plus swelling; 23 per cent had 2 plus swelling, and 26 per cent had ankle edema on the ligated side. Mild discomfort was reported by the same proportion of patients with ligation of the superficial femoral vein as was reported after ligation of the common femoral, but severe pain was present in only 3 per cent.

In the smaller group of patients with ligations of the vena cava, swelling of the entire leg was prominent in only 10 per cent, but 60 per cent of these patients had some swelling of the calf and ankle. None of them experienced disabling discomfort in spite of the swelling.

A similar follow-up study concerned 81 patients with thromboembolism in whom the anticoagulants were employed. The results are

included in chart 8. It is apparent that patients treated with anticoagulants also have post-thrombotic sequelae, although comparison with chart 7 illustrates the decreased frequency of severe swelling and pain when the anticoagulants are used rather than in ligation.

It is certainly not felt that the consideration of post-thrombotic swelling of the leg is the most important factor in the management of

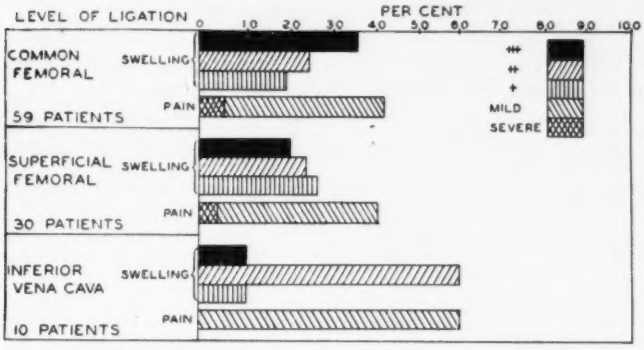

Chart 7.—Complications more than six months after venous ligation.

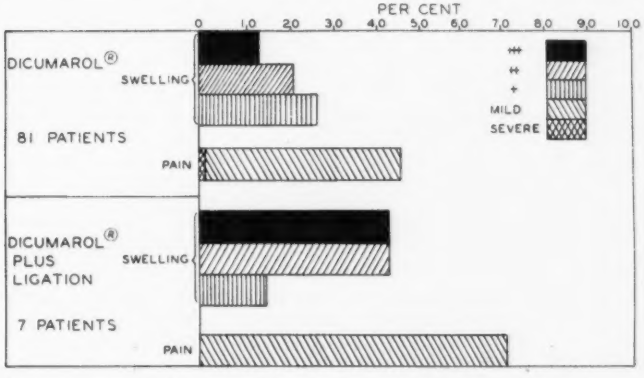

Chart 8.—Complications more than six months after anticoagulant therapy.

thromboembolism. However, we do believe that the administration of anticoagulants, whenever possible, and the use of venous ligation as a supplementary or alternate procedure in the special situations that have been described will result in the greatest protection from embolism with the least delayed discomfort to the patient.

SUMMARY

1. Experience in the management of thromboembolism at the University Hospital during the past nine years indicates that at present use of anticoagulants is the treatment of choice.

2. The value of interruption of a vein in thromboembolism is apparent in situations in which the anticoagulants are undesirable because of the lack of facilities for their control or of the special risk they represent for certain patients.

3. Anticoagulants and venous ligation have proved effective, in our experience, when employed along with general preventive measures in reducing the incidence of pulmonary embolism.

4. Further reduction in the occurrence of pulmonary embolism may be expected when these procedures are applied early in thromboembolism and when they are extended to the susceptible patient prior to the development of thrombosis or embolism.

5. The sequelae of venous thrombosis were less severe after use of anticoagulants than they were after venous ligation in the patients studied.

EARLY AND LATE SEQUELAE OF THERAPEUTIC VEIN LIGATION FOR THROMBOSIS OF VEINS OF LOWER LIMBS

D. EMERICK SZILAGYI, M.D.
AND
JOSEPH F. ALSOP, M.D.
DETROIT

WHILE excellent results have been reported with the use of both anticoagulant therapy and vein interruption in the treatment of postoperative thromboembolism,[1] a wider experience with their application will have to be gathered before the comparative merits of these two methods can be definitely stated. In any such evaluation the presence,

From the Department of Surgery of the Henry Ford Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. (*a*) Veal, J. R.: High Ligation of the Femoral Vein in Amputations of the Lower Extremities, J. A. M. A. **114**:1616 (April 27) 1940. (*b*) Sears, J. B.: Experience with Femoral-Vein Ligation for Prophylaxis of Postoperative Pulmonary Embolism, New England J. Med. **224**:108 (Jan. 16) 1941. (*c*) Homans, J.: Exploration and Division of the Femoral and Iliac Veins in the Treatment of Thrombophlebitis of the Leg, ibid. **224**:179 (Jan. 30) 1941. (*d*) Welch, C. E., and Faxon, H. H.: Thrombophlebitis and Pulmonary Embolism, J. A. M. A. **117**: 1502 (Nov. 1) 1941. (*e*) Lowenberg, E. L.: Femoral Vein Ligation in the Treatment of Pulmonary Embolism Due to Femoral Thrombophlebitis, Virginia M. Monthly **71**:288 (June) 1944. (*f*) Fine, J., and Starr, A.: The Surgical Therapy of Thrombosis of the Deep Veins of the Lower Extremities, Surgery **17**:232 (Feb.) 1945. (*g*) Veal, J. R., and Hussey, H. H.: Surgery of Deep Venous Thrombosis of the Lower Extremity, ibid. **17**:218 (Feb.) 1945. (*h*) O'Neil, E. E.: Ligation of the Inferior Vena Cava in the Prevention and Treatment of Pulmonary Embolism, New England J. Med. **232**:641 (May 31) 1945. (*i*) Gaston, E. A., and Folsom, H.: Ligation of the Inferior Vena Cava for the Prevention of Pulmonary Embolism: A Report of Two Cases, ibid. **233**:229 (Aug. 23) 1945. (*j*) Pratt, G. H.: Surgical Management of Thrombosis and Thrombophlebitis with Discussion of Vein Resection, New York State J. Med. **46**:1825 (Aug. 15) 1946. (*k*) Homans, J.: Medical Progress: Diseases of Veins, New England J. Med. **235**:163 (Aug. 1) 1946. (*l*) Moses, W. R.: Ligation of the Inferior Vena Cava or Iliac Veins, ibid. **235**:1 (July 4) 1946. (*m*) Hershey, C. D., and Bailey, R. B.: Vein Ligation in Thrombophlebitis, South. M. J. **39**:804 (Oct.) 1946. (*n*) Allen, A. W.: Interruption of the Deep Veins of the Lower Extremities in the Prevention and Treatment of Thrombosis and Embolism, Surg., Gynec. & Obst. **84**:519 (April) 1947. (*o*) Veal, J. R.; Hussey, H. H., and Barnes, E.: Ligation of the Inferior Vena Cava in Thrombosis of the Deep Veins of the Lower Extremities, ibid. **84**:

(Footnote continued on next page)

extent and permanence of the early and late sequelae associated with each method will have to be carefully weighed.

As regards vein interruption, in spite of a rather large number of published accounts dealing with its use, accurate data on postligation complications and residuals are scarce.[2] A follow-up survey of even a relatively small series of cases would, therefore, seem useful. Such a survey forms the main subject of this study. In addition to an analysis

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605 (April 15) 1947. (*p*) Donaldson, G. A.: The Therapy and Prophylaxis of Venous Thrombosis and Pulmonary Embolism, Surg. Clin. North America. **27:** 1037 (Oct.) 1947. (*q*) Linton, R. R., and Hardy, I. B.: Postthrombotic Sequelae of the Lower Extremity: Treatment by Superficial Femoral Vein Interruption and Stripping of the Saphenous Veins, ibid. **27:**1171 (Oct.) 1947. (*r*) Homans, J.: Venous Thrombosis and Pulmonary Embolism, New England J. Med. **236:**196 (Feb. 6) 1947. (*s*) Pratt, G. H.: Surgical Management of Venous Clotting, S. Clin. North America **28:**341 (April) 1948. (*t*) McClure, R. D., and Lam, C. R.: Experiences in Heparin Administration, J. A. M. A. **114:**2085 (May 25) 1940. (*u*) Lam, C. R.: Heparin Administration: Methods and Results in Thirty Cases, Am. Surg. **114:**205 (Aug.) 1941. (*v*) Bauer, G.: Venous Thrombosis, Arch. Surg. **43:** 462 (Sept.) 1941. (*w*) Jorpes, E.: Pure Heparin for the Prevention and Treatment of Thrombosis, Acta med. Scandinav. **107:**107, 1941. (*x*) Wetterdall, P.: The Use of Heparin as a Prophylactic against Thrombosis Following Gynecologic Operations, ibid. **107:**122, 1941. (*y*) Crafoord, C.: Heparin as a Prophylactic Against Postoperative Thrombosis, ibid. **107:**116, 1941. (*z*) Bauer, G.: Heparin and Venous Thrombosis, J. A. M. A. **131:**196 (May 18) 1946. (*a'*) Ziliacus, H.: The Results of Five Years' Treatment of Thrombosis and Pulmonary Embolism at a Series of Swedish Hospitals During the Years 1945 to 1946, Acta med. Scandinav. (supp.) **171:**1, 1946. (*b'*) Jorpes, E.: Anticoagulant Therapy in Thrombosis, Surg., Gynec. & Obst. **84:**677 (April 15) 1947. (*c'*) Murray, G.: Anticoagulants in Venous Thrombosis and the Prevention of Pulmonary Embolism, ibid. **84:**665 (April) 1947. (*d'*) Evans, J. A., and Boller, R. J.: The Prevention of Postoperative Pulmonary Embolism, New England J. Med. **236:**392 (March 13) 1947. (*e'*) Cosgriff, S. W.; Cross, R. J., and Habif, D. V.: The Management of Venous Thrombosis and Pulmonary Embolism, S. Clin. North America **29:**324 (April) 1948. (*f'*) Barker, N. W.; Cromer, H. E.; Hurn, M., and Waugh, J. M.: The Use of Dicumarol in the Prevention of Postoperative Thrombosis and Embolism with Special Reference to Dosage and Safe Administration, Surgery **17:**207 (Feb.) 1945. (*g'*) Deleted on proof. (*h'*) Smith, G. V. S., and Milligan, W. J.: Dicumarol Prophylaxis Against Venous Thrombosis in Women Undergoing Surgery, Surg., Gynec. & Obst. **86:**461 (April) 1948. (*i'*) Shlevin, E. L., and Lederer, M.: Uncontrollable Hemorrhage after Dicoumarol Therapy with Autopsy Findings, Ann. Int. Med. **21:**332 (Aug.) 1944. (*j'*) Loewe, L.; Hirsch, E.; Grayzel, D. M., and Kashdan, F.: The Action of Heparin in Experimental Venous Thrombosis, Surgery **22:**746 (Nov.) 1947. (*k'*) Kiesewetter, W. B., and Shumacker, H. B. Jr.: An Experimental Study of the Comparative Efficacy of Heparin and Dicumarol in the Prevention of Arterial and Venous Thrombosis, Surg., Gynec. & Obst. **86:**687 (June) 1948.

2. Northway, R. O., and Buxton, R. W.: Ligation of the Inferior Vena Cava, Surgery **18:**85 (July) 1945. Ray, C. T., and Burch, G.: Vascular Responses in Man to Ligation of the Vena Cava, Arch. Int. Med. **80:**587 (Nov.) 1947.

of clinical observations, certain facts obtained by special roentgenograms of the extremities will be recorded.

MATERIAL

Clinical Characteristics.—The cases under study comprise all the operations of vein interruption performed in the Henry Ford Hospital from July 1, 1942 to Dec. 31, 1948 (table 1). The practices of the medical and surgical departments of the hospital in dealing with venous thrombosis during this time have undergone changes that mirror the trends in other places. Exact figures are not available, but less than half of the patients with thrombosis of the veins of the limbs during the period were treated by surgical interruption.

TABLE 1.—*Vein Interruptions, July 1, 1942 to Dec. 31, 1948.*

Total number of cases	100
Number of ligations	146
Surgical cases	77
Nonsurgical cases	23

TABLE 2.—*Surgical and Nonsurgical Conditions Associated with Venous Thrombosis*

	Number of Cases
A. Operative Procedures Preceding the Appearance of Thrombosis:	
Operations on spinal column	12
Hernioplasty	11
Fractures of and operations on leg	10
Cholecystectomy	8
Prostatectomy	6
Radical mastectomy	5
Traumatic injury of limb	5
Abdominoperineal resection of rectum	4
Gastrectomy	3
Hysterectomy	3
Splenectomy	2
Childbirth	2
Miscellaneous	6
B. Nonsurgical Diseases Associated with Thrombosis:	
Primary thrombophlebitis	12
Heart disease with congestive failure and auricular fibrillation	8
Carcinoma (inoperable) of lung	1
Uremia	1
Terminal carcinomatosis	1

One hundred patients were treated with vein interruption. In 77 cases the operation was done for postoperative thrombosis; in 23 cases the cause of the venous clotting was nonsurgical. In table 2 are listed the operations that preceded the appearance of venous involvement. It must be remarked that, since during the period covered by the study forms of treatment other than vein interruption were also used in different services, this tabulation does not reflect the true incidence of venous thrombosis. Of the nonsurgical patients, 16 were ambulatory at the time of appearance of symptoms and 7 were bedridden. The high incidence of cardiac disease (rheumatic and arteriosclerotic) with congestive failure and auricular fibrillation is worthy of note.

The sex and age distributions (table 3) conform with universally observed facts. It is worthy of emphasis that 77 per cent of the patients were over 40 years of age.

The clinical signs and symptoms are classified in tables 4 and 5.

It is significant that in 43 per cent of the cases the presenting sign or symptom was that of pulmonary embolism and that in 5 per cent more it consisted in advanced involvement of the limbs in the form of tenderness of the thigh (2 per cent) and edema of the leg (3 per cent) (table 4). These findings, together with the distribution of the signs and symptoms of the fully developed clinical picture (that includes an incidence of 55 per cent of embolic phenomena and of 23 per cent of

TABLE 3.—*Age and Sex Incidence*

Age, Years	Patients, Number	
21-30	7	
31-40	16	Average age: 51 yrs.
41-50	20	
51-60	27	(b) Males — 63 patients
61-70	19	
71	11	Females — 37 patients
Total	100	

TABLE 4.—*Distribution of Presenting Symptoms or Signs*

Symptom or Sign			Number of Cases
Calf, pain or tenderness			57
Chest	pain	5	43
	signs	38	
Leg, swelling			3
Thigh, pain or tenderness			2

TABLE 5.—*Distribution of Symptoms and Signs in the Established Clinical Picture*

Symptom or Sign	Number of Cases
Calf, pain or tenderness	88
Chest, pain or signs	52
Thigh, pain or tenderness	23
Hemoptysis	26

involvement of the thigh) (tables 5 and 6), indicate that in a high proportion of the patients treated the thromboembolic process was well advanced.

Table 6 merits comment on account of its negative qualities. The large number of incomplete examinations of the limbs speaks ill for the thoroughness of the house staff. It should be added, however, that most of the insufficient information dates from the first four years of the survey, when the present concept of the elusiveness of the clinical picture of thromboembolic disease had not yet become general knowledge.

In the latter years the attitude of uncompromising suspicion has been accepted by most of the staff of this hospital, and the examinations of the limbs have become frequent and painstaking.

An analysis of the evidence of pulmonary embolism (table 7) brings out a point that always bears stressing: Pulmonary embolism in a varying number of cases cannot be verified roentgenologically.

The meaning of table 8, showing the incidence of elevated temperature and pulse rate, is not entirely clear. While the lingering of postoperative fever and tachycardia or the appearance of an elevated temperature and

TABLE 6.—*Local Signs and Extent of Involvement*

	Present	Absent	Not Stated
A. Local Signs of Involvement of Veins			
Tenderness in calf	88	12	..
Tenderness in thigh	23	20	57
Plantar tenderness	6	12	82
Homans' sign	52	7	41
Edema	21	11	68

	No. of Cases
B. Extent of Clinical Involvement of Veins	
Calf	102
Calf and thigh	22
Thigh only	2
None	24

TABLE 7.—*Incidence of Pulmonary Embolism*

	Number of Cases
A. Total Incidence	55
B. Evidence of Pulmonary Infarction	
Clinical signs and symptoms	55
Roentgenographic evidence	40
C. Signs and Symptoms of Pulmonary Embolism	
Pain in chest	59
Signs in chest	43
Hemoptysis	26

pulse after a normal period, in general, are strong warnings of the possibility of venous thrombosis, in any individual case the persistence of the postoperative rise may be difficult to interpret. It seems undeniably important, however, that in 74 and 71 per cent of the cases studied the temperature and pulse rate, respectively, were above normal.

There is evidence [1b] that early postoperative rising reduces the incidence of postoperative venous clotting. That phlebothrombosis may occur in spite of early ambulation is also generally accepted. In this short series, in 11 patients out of 77 who were up and about on the day of their operation venous clotting developed; on the other hand, over half (50.7 per cent) of the patients had been kept in bed for over seven days postoperatively.

In view of the purpose of this study, the data contained in table 9 have special significance. There is ample proof that the time of inception of the treatment in relation to the time of onset of the symptoms of venous thrombosis has much bearing on the results of treatment with anticoagulants [3]; the earlier the diagnosis and the prompter the treatment, the better are the results, both as to local residuals and as to prevention of embolism. It is reasonable to assume that this is probably true also in regard to treatment with vein interruption. Thus it is meaningful that the lapse of time between the appearance of the first symptom or sign and the time of treatment in this series (table 9) averaged six days after operation and eighteen days when operation was not performed.

TABLE 8.—*Pulse Rate and Temperature*

	Number of Cases
A. Temperature	
99 — 100 F.	19
100 plus F.	55
B. Pulse	
10 —100 min.	29
100 plus min.	42

TABLE 9.—*Interval Between Time of First Symptom or Sign of Venous Thrombosis and Time of Ligation*

Interval, Days	Number of Cases
Less than 1	19
1-2	27
3-7	22
8-14	17
15-28	12
Over 28	3

Several factors contributed to the delay in the institution of treatment. In the medical cases throughout the entire period surveyed the tendency has been to try conservative management first and to resort to surgical treatment only if the course was not favorably influenced. As regards postoperative venous thrombosis, the same point of view prevailed in some of the earlier cases, whereas in many others (in the first years of the period covered) diagnosis was not conclusively made until advanced signs appeared. In the surgical services, during the last four years the outlook has radically changed and no time is lost before starting the treatment. Nevertheless, the length of the "waiting time" for the entire group of cases remains excessively high. This fact, together

3. Bauer,[1v,z] Jorpes.[1b']

with the other evidence, already given, of the advanced character of a large portion of these cases, must be borne in mind when judgment is made of the postligation sequelae.

Types of Vein Interruption.—In the 100 cases 146 procedures of vein interruption were carried out. The classification of these operations is shown in table 10. All but 5 of the procedures were ligations in continuity. In 2 of the early cases the vein (in both cases the common femoral) was opened and the clot, as far as possible, removed. In 3 instances the vein (the common femoral) was opened in order to ascertain the absence or presence of clotting at the exposed level, and, a thrombus not having been found, the vein was tied. Early we reached the decision that removal of the clot was not a reliable procedure, chiefly because of the probability of the reformation of the clot in the vein segment whose intima had been damaged at the site of thrombosis and further insulted by the operative intervention. Concerning the site of ligation, in the earlier

TABLE 10.—*Classification of Operations*

	Number of Cases
A. Type of Operation	
Ligation in continuity	141
Section and ligation	3
Thrombectomy and ligation	2
B. Level of ligation (number of cases)	
Unilateral	
Left superficial femoral	21
Right superficial femoral	20
Left common femoral	3
Right common femoral	4
Left common iliac	1
Right common iliac	1
Bilateral	
Superficial femoral	41
Common femoral	2
Left common femoral with right superficial femoral	2
Left common iliac with right superficial femoral	1
Vena cava ligation	4

cases much experimentation had to be done. Eventually the following principles of conduct were accepted.

If the clinical involvement is limited to the popliteal vein or to levels below, the common femoral vein is exposed through a subinguinal incision. (The incision is usually parallel to the inguinal crease, being placed 2 cm. distal to it and centered on the femoral pulsation. However, a good many longitudinal incisions were also employed. Provided care is taken not to injure the subinguinal lymphatic nodes there seems to be little to choose between the two types of approach; wounds made in either way healed without a single important complication.) During the exposure and dissection, the greater saphenous vein is used as a guide to the femoral sheath and its branches are carefully saved. Enough of the femoral trunk is brought into view to determine the site of embouchure of the deep femoral vein or one of the deep circumflex femoral veins. Our impression at the operating table, confirmed by anatomic studies of others,[4] has been that the topographic disposition of the deep femoral vein is quite variable and that often it joins the superficial femoral vein at levels so low

4. Edwards, E. A., and Robuck, J. D., Jr.: Applied Anatomy of the Femoral Vein and its Tributaries, Surg., Gynec. & Obst. **85**:547 (Nov.) 1947.

that its operative visualization entails a forbidding amount of dissection. Therefore, if along an 8 or 10 cm. segment of the main femoral trunk a definite vena profunda femoris is not found, a circumflex vein (either medial or lateral) not less than 1 cm. in diameter is selected as the site of ligature. An operative detail of utmost importance is the placing of the ligature distal but as close to such a branch as possible without encroaching on its lumen. In this manner one probably prevents the formation of a stagnant column of blood in the segment of vein directly proximal to the ligature. Operations done in this manner have been listed by us as ligations of the superficial femoral vein, although in a small number of cases the level of ligation may, in fact, have been proximal to the profunda femoris branch. Clinically the difference cannot be detected.

The material used for ligation has been 00 (U. S. P.) braided silk; two ligatures are placed 0.5 cm. apart. The placing of the ligature is always preceded by a careful inspection and palpation of the exposed segment of the vein. We believe that it is possible to determine the absence of clotting in the vast majority of cases. If there is any doubt, the venous trunk is opened. If there is thrombosis but a segment of the common femoral trunk distal to the greater saphenous vein is free from it, the ligation is carried out at that level. If the thrombosis has extended to a level proximal to the saphenofemoral junction, ligation below the inguinal ligament is thought ill advised.

Whenever there is a choice, therefore, we favor ligation of the superficial femoral vein in the sense just mentioned. Ligation of the common femoral vein is reserved for cases of thrombosis extending proximal to the highest circumflex branch but leaving the saphenofemoral junction free. In clinical practice the uppermost limit of thrombosis is difficult to determine and the decision whether to use one or the other level is usually made at the operating table. After several femoral explorations, we have learned that when the clinical evidence of thrombosis suggests involvement of the common femoral vein, it is wiser to ligate above the external iliac level. When this circumstance occurs on one side, with the other side entirely uninvolved, it constitutes our only indication for ligation of the common iliac vein.[5] If the condition is present bilaterally, ligation of the vena cava is the procedure of choice. Aside from using it in cases of bilateral involvement of the entire femoral venous system, we have resorted to ligation of the vena cava also in cases with definite evidence of pelvic venous thrombosis.

In the earlier cases of the series, interruption of the vein was limited to the extremity that was clinically judged to be involved. Increasing experience both in our hospital and elsewhere soon taught us that unilateral ligation carries an appreciable risk, even if the opposite limb is watched with especial care. Examples of instances in which unilateral ligation proved dangerously inadequate will be given subsequently. At present, bilateral ligation is performed in every case, regardless of the limitation of clinically evident signs to one side.

Anticoagulant Therapy and Vein Ligation.—There is no *a priori* reason for opposing anticoagulant therapy as a measure adjuvant to vein interruption. We have attempted, however, to rely on vein ligation alone as often as practicable in order to be better able to evaluate its worth. In a few cases resort had to be made to the use of anticoagulant drugs to treat embolic complications following ligation; these cases will

5. Such an operation is always accompanied with a prophylactic contralateral ligation of the superficial femoral vein.

be discussed presently. In 7 cases heparin and in 1 case dicumarol,* in full therapeutic doses, either failed to prevent embolism or caused serious complications and had to be supplanted by ligation. In a number of instances, and mainly in other services, anticoagulant drugs were administered in nontherapeutic doses in conjunction with ligation, for questionable reasons (table 11). Since the postoperative dosage in these cases was not fully therapeutic, the effect of the drugs on the ultimate results of vein ligation may be disregarded. A separation of the cases in which some partial effect may have been brought about is impossible for practical reasons.

RESULTS

The therapeutic results of vein interruption can be evaluated from two points of view: that of its success in preventing pulmonary embolism and that of its effect on the subsequent evolution of the local thrombotic process.

Prevention of Pulmonary Embolism.—Taking all cases, 8 operations were followed by pulmonary embolic episodes (table 12). A brief

TABLE 11.—*Anticoagulant Drugs and Ligation*

	Number of Cases
A. Anticoagulant drugs used	
Because of failure of ligation	1
To complement ligation	20*
B. Ligation done because of failure of anticoagulants	7

* Nontherapeutic doses administered in 18 cases.

review of these cases is instructive. In the first 5 cases unilateral ligation was done; in the last 3, bilateral ligation.

CASE 1.—M. B. had traumatic thrombophlebitis of the left leg, followed by pulmonary embolism one month later. Ligation of the right superficial femoral vein was done on April 6, 1943. One month later (while bedfast) the patient had another pulmonary infarct, and dicumarol® therapy was instituted. The patient recovered.

CASE 2.—J. A. had primary phlebothrombosis of the right leg with pulmonary infarct treated for three weeks as pneumonia. On Jan. 30, 1944 signs of phlebothrombosis of the right common femoral vein appeared. The right common iliac vein was ligated immediately. Another pulmonary infarct occurred on February 5 and was followed by ligation of the left superficial femoral vein. Recovery was uneventful.

CASE 3.—J. M. underwent complete hysterectomy on May 1, 1944. On the fourteenth postoperative day pulmonary embolism with mild signs of phlebothrombosis in the left leg developed. The left superficial femoral vein was ligated on May 17 and the patient was discharged improved. On readmission, July 1, there were evidence of pulmonary embolism and a slight clinical suggestion of phlebothrombosis in the right leg. The right superficial femoral vein was immediately ligated and the patient recovered.

CASE 4.—C. R., with primary thrombophlebitis of the right leg, underwent ligation of the right superficial femoral vein on Aug. 23, 1946. Pulmonary embolism occurred on September 6. Ligation of the left superficial femoral vein was done immediately. The patient recovered.

CASE 5.—A. C., with rheumatic heart disease with congestive failure and auricular fibrillation, was admitted to the hospital after repeated episodes of pulmonary embolism. On the indication of tenderness in the right calf, the right superficial femoral vein was ligated on Aug. 23, 1946. The patient was discharged improved but six weeks later was readmitted with signs of new pulmonary infarct. Death occurred on the day of admission before treatment could be given. Autopsy was not done.

CASE 6.—A. S., who had rheumatic heart disease with congestive failure and auricular fibrillation, was admitted with recent pulmonary infarct and questionable clinical signs of phlebothrombosis in the right calf. Bilateral ligation of the superficial femoral vein was done on Oct. 15, 1946. The patient died suddenly of pulmonary embolism seven days later. At autopsy many pulmonary infarcts of various ages were observed. The source of the embolism was not found (probably the heart; the legs were not dissected out, but the pelvic veins were normal).

TABLE 12.—*Pulmonary Embolism After Ligation*

		Number of Cases
Embolism following unilateral operation		5*
Treated with anticoagulant drug	1	
Treated with ligation	3	
Embolism following bilateral operation		3*
Treated with anticoagulant drug	2	
Nonfatal embolism attributable to failure of ligation		1
Fatal embolism attributable to failure of ligation		0

* Treatment not administered in 1 case.

CASE 7.—F. B., with sickle cell anemia with hemolytic crises, underwent splenectomy on June 13, 1947. Signs of pulmonary embolism were noted on the sixth postoperative day without definite localization of the source of the embolism. Six days later bilateral ligation of the superficial femoral vein was done. Three days later another pulmonary embolism occurred. Heparin and dicumarol® therapy was begun, and the patient recovered.

CASE 8.—H. N. underwent gastroenterostomy with bilateral subdiaphragmatic vagal neurectomy on Nov. 1, 1947. Evidences of phlebothrombosis involving the right common femoral vein were noted one week later. The right common iliac vein was ligated immediately. The patient was discharged improved and made uneventful progress for eleven and a half months postoperatively, when (while the patient was at home out of town) pain in the left leg appeared. On return to the hospital on Nov. 20, 1948 there was clinical but no roentgenologic evidence of pulmonary embolism. Ligation of the left superficial femoral vein was done immediately. The patient was discharged improved, but three weeks after the second ligation a massive pulmonary embolus occurred while the patient was at home (out of town). Treatment with heparin was followed by recovery.

In how many of these cases may one rightfully ascribe the failure to prevent embolism to the inherent shortcomings of ligation as a method of treatment?

The first step in looking for an answer must be the examination of the indications for the use of vein interruption in each case. It is readily seen that in cases 5, 6 and 7 the source of embolism was not clear. In cases 5 and 6 (both cases of rheumatic heart disease with congestive failure) in particular there was little justification for expecting any benefit from vein ligation; as the final outcome strongly suggests, both these patients had emboli from the right side of the heart.

The next point of inquiry concerns the question whether, if ligation was indicated, the correct procedure was chosen. In this respect it is noted that, leaving case 8 aside as a special problem to be discussed presently, in all the remaining cases ligation was unilateral and that in all these cases in which a second ligation was resorted to the embolic episodes were satisfactorily controlled. This fact would therefore suggest that the failure of the first ligation was due to the incompleteness of the procedure for the given situation rather than to any immanent fault of the method.

The last case (case 8) is difficult to analyze. The first operation (ligation of the right common iliac vein) apparently was adequate to treat the thrombosis, for the patient progressed very well for almost a year. The second ligation (of the left superficial femoral vein) again seemed sufficiently radical, since no thrombosis of the common femoral vein was found on exploration. When the latter procedure was followed in a week by a grave episode of pulmonary embolism, we assumed that a clot must have formed proximal to the point of ligation and broken away. This assumption was proved incorrect, however, when, two months after the last embolic incident, phlebograms showed the left common femoral vein to be well filled. It must be further theorized that this patient has had—perhaps still has—a nidus of thrombosis outside the principal venous trunks draining the limbs, possibly in the pelvis.

In summary, therefore, one can state that vein interruption affords a very high degree of safety for the prevention of the embolic complications of thrombosis, provided the operative indications are correct, the level of the ligation high enough and the operation bilateral. Excluding the instances of inadequate operation (4 cases) and grossly erroneous choice of methods (3 cases), we encountered only 1 case (case 8) in which interruption of the vein above the level of thrombosis failed to give full protection against embolism.

Effect on the Local Pathologic Process.—The second aspect of the analysis of the results of vein interruption is concerned with the effects of the procedure on the local thrombotic process. This phase of the inquiry can be conveniently divided into the examination of the immediate results and that of the late sequelae.

Early Effects: In table 13 are listed the observations made on the appearance of (if none was previously present) or increase in the swelling of the limbs after ligation. These data are either translations of actual preligation and postligation measurements of the extremities or interpretations of the progress notes on the records. It is evident that swelling occurs in at least 80 per cent of the limbs operated on. Clinically the swelling appears to have two components: venous congestion and interstitial exudation (edema). At times the swelling is associated with aching pain and tenderness; at others, it is entirely symptomless.

The opinion is generally held that the swelling is commoner and more pronounced in cases in which the extent of the thrombosis already established at the time of ligation is greater. This is our impression also, although our statistical data are not entirely convincing on this point. It would be wrong, however, to interpret this fact as proof (as

TABLE 13.—*Incidence of Early Postligation Swelling of the Limb*

Degree of Swelling	Number of Limbs	Percentage of Total
None	10	7
Slight	48	32
Moderate	62	41
Severe	10	7
Not stated	20	13

has been done by some) that the degree of postligation swelling is determined solely by the degree of preexisting thrombosis. Obviously, an increase in the swelling (or the appearance of swelling) can be postulated to take place either if there is no extension of thrombosis after ligation but by the ligation certain important drainage channels are shut off, or if after ligation the thrombotic process grows more extensive and, in addition to the surgical blocking of the venous return, it further reduces the available return pathways. Which of these two possibilities or what combination of them actually happens in a given case is impossible to say at present. We attempted a statistical evaluation of our cases in this respect, but our data are insufficient to allow any conclusion. Indeed, even a very large number of cases, with accurate and frequent measurements of limbs, would probably be of doubtful value for answering the question. Evidently methods other than clinical observation and measurement must be resorted to. In paragraphs to follow a brief account will be given of our experience with phlebography which has given promise of elucidating at least some phases of this problem.

The question of postoperative swelling has, of course, more than theoretic interest. As the precursor of the late sequelae, it must be taken into serious account whenever the advantages and disadvantages of vein ligation are weighed.

Late Sequelae: We attempt to follow our patients with vein ligation indefinitely in the clinic. It has been possible to maintain contact until the present with well over half of the patients. Over 20 per cent more were repeatedly examined in the past for periods of three months to three years after their operations before they either died or dropped out of sight. Seven patients have kept us up to date on their condition by correspondence. Thus we have satisfactory records of progress for

TABLE 14.—*Success of Follow-Up*

Method of Follow-Up	Number of Cases*
Current clinic visits	66
Current correspondence	7
Clinic visits in the past (3 mo. to 3 yr.)	23
None	4

* Fifteen patients are dead of causes unrelated to the operation on the vein.

TABLE 15.—*Length of Follow-Up*

Length of Follow-Up, Years	Percentage of Total Cases Followed
1/12-½	15.5
7/12-1	8.7
2-3	50.0
4-5	20.1
6-7	5.2

* Four cases (4 per cent of total) were lost from observation.

a year or more in 76 per cent of the cases in which we operated. In tables 14 and 15 are listed the details of the extent and length of the follow-up.

The establishment of objective, or at least reliable, criteria for the appraisal of the functional condition of a formerly diseased limb is a very difficult task. We chose for our follow-up examinations the following graded functional classification: "Sequelae absent": no swelling at rest or exercise; no complaint for which objective explanation can be found; physical condition of the limb normal; measurements (circumference of the ankle just above the inner malleolus, of the calf at its largest girth and of the thigh 20 cm. above the upper border of the patella) normal. "Sequelae slight": no swelling at rest, slight swelling on exercise; no complaint (as in preceding classi-

fication); physical condition of the limb normal at rest, with slight edema on exercise; measurements normal. "Sequelae moderate": slight edema at all times, made worse by exercise; bandage or elastic hose worn; complaint of aching fulness of moderate degree on exercise; slight degree of varices, induration or edema of the leg; measurements no more than 2 cm. above those normal for the patient (when these are known). "Sequelae severe": definite edema at rest, much aggravated by exercise, and use of a bandage or elastic hose obligatory; complaint of severe aching, fulness or claudication; prominent varices, pronounced induration, static dermatitis or ulceration; measurements more than 2 cm. above normal.

While these categories of classification are arbitrary, the criteria on which they are based were applied as uniformly and objectively as the nature of the investigation permitted.

Table 16 summarizes the findings in the limbs when last seen.

TABLE 16.—*Late Sequelae of Vein Ligation*

Classification of Sequelae	Number of Limbs	Percentage of Total
Absent	50	33
Slight	52	35
Moderate	39	26
Severe	2	1
No follow-up	7	5

Before we attempt a comprehensive appraisal of the results, some remarks on observations made during the follow-up periods seem to be in order.

When watching the progress of these patients one is soon impressed with the importance of the attention the patient is willing or able to apply to the care of the limbs. Simple measures of physical therapy (massage and exercises), the conscientious use of elastic bandages or hose whenever swelling appears, prompt treatment of cutaneous lesions and avoidance of trauma of any kind contribute remarkably to the rehabilitation of the extremity. Restitution to normal of some of the limbs that were extensively involved at the time of ligation often has been surprisingly complete. On the other hand, in several of the cases with more pronounced sequelae the functional impairment of the leg was due not so much to the ravages of venous thrombosis as to the neglect in the care of the limbs. One of the patients classified as having sequelae of severe degree and who has a static ulcer is entirely remiss in attending to the care of his leg.

Every limb followed showed progressive improvement after the first month after ligation, provided the necessary minimum care was

taken by the patient. Clinically at least, the formation of collaterals appears to be well advanced by this time in the majority of cases. Improvement may go ahead for as long as a year, after which little change for the better is noted. Seemingly the hemodynamic adjustments reach their peak at the end of this period.

A special word may be said regarding the cases of ligation of the vena cava. Two of the patients have moderate and 2 slight residuals; all 4 continue their previous occupations (they are all housewives) without serious handicap other than the demands of the special care of their limbs. All 4 originally had very extensive pelvic thromboses with sublethal pulmonary emboli.

The current concepts of the mechanism of physiologic restitution after phlebothrombosis have been repeatedly described,[6] and our clinical studies can add to them nothing new. (Some observations made in studying the phlebographic appearances of these limbs will be described in subsequent paragraphs.)

TABLE 17.—*Relationship of Preligation Involvement to Late Sequelae*

N. B. 120 limbs evaluated		Incidence of Late Sequelae, Percentage of Total			
Extent of Involvement	Number of Limbs	None	Slight	Moderate	Severe
None	20	50	19	31	0
Calf	79	28	40	32	0
Thigh	20	24	33	33	10

The relationship of the degree of preligation thrombosis to the severity of early swelling after vein interruption has been mentioned. In table 17 the grouping of late sequelae in relation to the original degree of vein involvement, as judged clinically, is given. While the number of cases is too small to allow valid statistical conclusions, the trend of evidence seems to confirm the assumption that the more extensive the thrombotic process the severer are the sequelae.

Since there is available no like series of cases of venous thrombosis treated with anticoagulants or with the methods (largely useless) popular before the advent of anticoagulants or vein interruption, a comparative appraisal of the results is not possible. Without any claim to superiority for the method, it can be said, however, that in this group of ligations, comprising a high proportion of operations for advanced venous thrombosis, the condition of a third of the limbs has returned to normal, that the condition of another third has improved enough to

6. Veal, J. R., and Hussey, H. H.: The Pathologic Physiology of the Circulation in Acute, Thrombophlebitis and the Postthrombotic Syndrome, Am. Heart J. **23**:390 (March) 1942. Bauer.[17]

be no more than a slight inconvenience to the patient and that even in the least satisfactory cases it has not interfered with the pursuit of a normal and useful life.

PHLEBOGRAPHY

As mentioned earlier, the evolution of the process of clotting in the veins of the limb after ligation is impossible to follow accurately by purely clinical means. The visualization of the venous system of the lower extremity with the help of a radiopaque dye seemed to us to offer a more promising method for this purpose.

Technic of Phlebography.—We have used phlebography in the past sporadically as a diagnostic aid in venous thrombosis with rather indifferent results. Our impression had been that in the conventional technics [7] a number of factors that determine the passage of the dye into the deep veins of the leg and thence into the venous system of the thigh are uncontrolled. Thus parts of the deep system may remain unfilled by the dye and may be wrongly interpreted as pathologically obstructed. In our inquiry there was also another technical difficulty to overcome: the simultaneous complete visualization of the venous systems of both the leg and the thigh. In the technics formerly described, because of the smallness of the quantity of dye introduced

7. Franklin, K. J.: A Monograph on Veins, Springfield, Ill., Charles C Thomas, Publisher, 1947. Bauer, G.: Venographic Studies of Thromboembolic Disease, Acta chir. Scandinav. (supp. 61) **84**:1, 1940. Starr, A.; Frank, H. A., and Fine, J.: The Venographic Diagnosis of Thrombophlebitis of the Lower Extremities, J. A. M. A. **118**:1192 (April 4) 1942. Welch, C. E.; Faxon, H. H., and McGahey: The Application of Phlebography to the Therapy of Thrombosis and Embolism, Surgery **12**:163 (Aug.) 1942. Luke, J. C.: Retrograde Venography of Deep Leg Veins, Canad. M. A. J. **49**:86 (Aug.) 1943. Baker, E. C., and Sedwitz, S. H.: Observations on Venography of the Lower Extremities, Radiology **41**:451 (Nov.) 1943. DeBakey, M. E.; Schroeder, G. F., and Ochsner, A.: Significance of Phlebography in Phlebothrombosis, J. A. M. A. **123**:738 (Nov. 20) 1943. Baker, E. C., and Miller, F. A.: Further Experiences with Venography, Radiology. **43**:129 (Aug.) 1944. Papper, E. M., and Imler, A. E.: Use of Phlebography and Lumbar Sympathetic Block in the Diagnosis of Venospasm of the Lower Extremity, ibid. **15**:402 (March) 1944. Lesser, A., and Danelius, G.: Venography: Its Value in the Diagnosis and Management of Venous Disturbances of the Lower Extremities, Ann. Surg. **119**:903 (June) 1944. Oliver, C.: Phlébographie et phlébectomie dans les phlébitis postoperatoires récentes et profondes du membre inferieur, Presse méd. **53**:132 (March 17) 1945. Farinas, P. L.: Abdominal Venography, Am. J. Roentgenol. **58**:599 (Nov.) 1947. O'Laughlin, B. J.: Roentgen Visualization of the Inferior Vena Cava, ibid. **58**:617 (Nov.) 1947. Bull, D. C.: Phlebography of Lower Extremity, S. Clin. North America **28**:541 (April) 1948. Allen, E. G.; Hines, E. A., Jr.; Walter, P. O.; Kavle, F., and Barker, N. W.: The Use of Dicumarol as Anti-Coagulant: Experience in 2307 Cases, Ann. Int. Med. **27**:37 (Sept.) 1947.

and also because of the way of introduction, the veins of the thigh and lower part of the pelvis are seldom filled (even if the veins of the legs are well outlined); the dye is usually too diluted when it reaches the upper segments of the venous system of the thigh to give a sharp shadow.

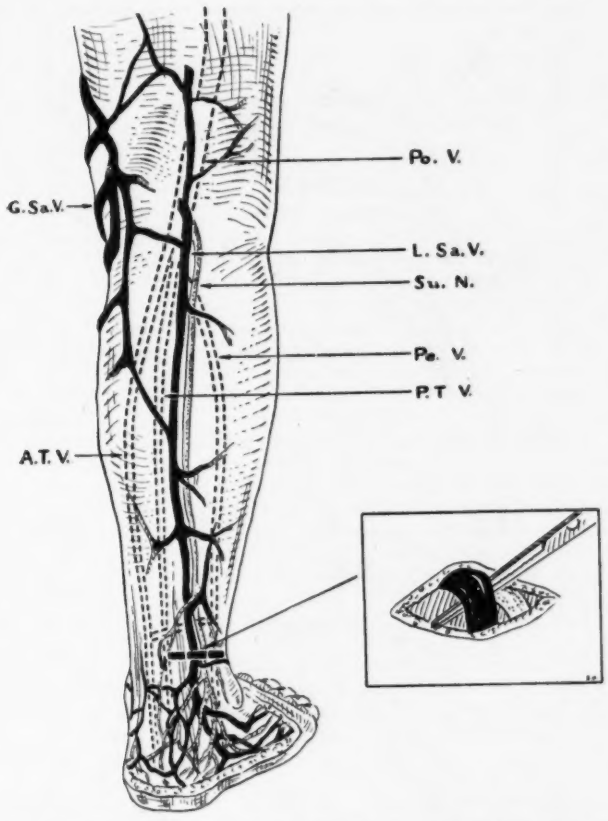

Fig. 1.—Sketch of the right leg showing the relationships of the lesser saphenous vein to the popliteal vein and sural nerve. The site of incision is marked with heavy broken lines running from the lateral malleolus to the border of the achilles tendon. *Po.V.* indicates the popliteal vein; *G.Sa.V.*, the greater saphenous vein; *L.Sa.V.*, the lesser saphenous vein; *Su. N.*, the sural nerve; *Pe.V.*, the peroneal vein; *P.T.V.*, the posterior tibial vein; *A.T.V.*, the anterior tibial vein.

After numerous trials with modifications of earlier technics, the following procedure was worked out (figs. 1 and 2).

With the patient prone, a 1 cm. long incision is made over the lesser saphenous vein slightly proximal to the point where it is formed by its tributaries from the foot. The location of the incision is shown in figure 1. If a transverse line is drawn from the upper border of the malleolar prominence of the fibula to the lateral border of the achilles tendon and this line is divided into three equal

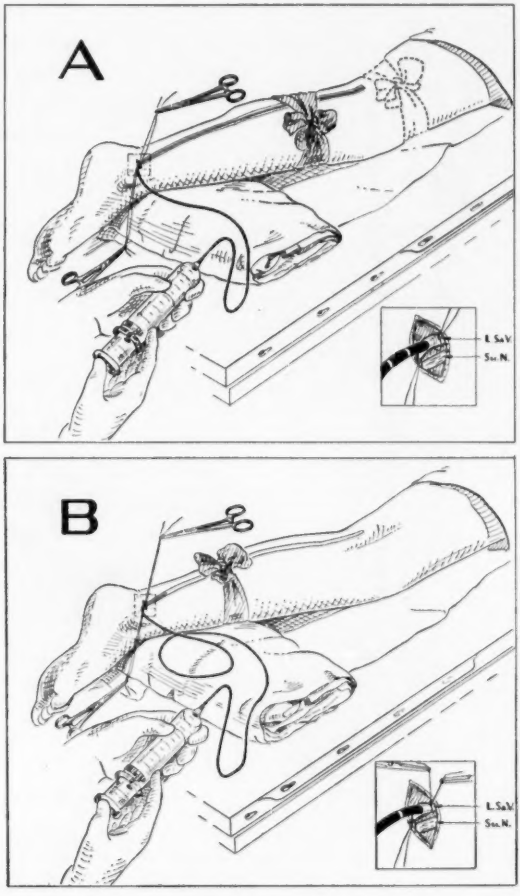

Fig. 2.—The technic of phlebography. *A*, catheter in the lesser saphenous vein, reaching as far as the saphenopopliteal junction. Radiography of the lower pelvis and upper three fourths of the thigh. (The use of the proximal tourniquet is not always necessary.) *B*, the tip of the catheter has been withdrawn to a point 4 to 5 cm. proximal to the site of phlebotomy. This phase of the procedure visualizes the upper three fourths of the leg and the lower one third of the thigh. (X-ray tube omitted from sketch.)

segments, the middle third of the line corresponds to the site of the incision. The lesser saphenous vein is in the posterior half of the incision (the half nearer the achilles tendon). The sural nerve runs deep and slightly lateral to the vein in very close proximity. Every precaution must be taken to avoid injuring or handling the sural nerve during the procedure. Between two holding ligatures of 000 plain surgical gut, only the distal one of which is tied at this time, a small incision is made into the wall of the vein and a no. 6 or 7 woven ureteral catheter[8] is introduced into the vessel. A length of the catheter is passed that has been formerly determined by measuring the distance between the proposed site of incision and the popliteal crease, the latter corresponding to the level of the point of junction of the lesser saphenous and popliteal veins (a very constant anatomic landmark). Introducing the catheter farther up (into the popliteal vein) requires fluoroscopic control and is not necessary. With the catheter in place, the blood pressure in the saphenous system is now determined.[9] Two tourniquets have been previously put in place untied, one 5 to 8 cm. above and one the same distance below the level of the popliteal crease; these tourniquets are now tied under sufficient tension to dimple the skin. The x-ray tube is so centered that a view is obtained of the lower part of the pelvis and the upper three fourths of the thigh on a 14 by 17 inch (35 by 43 cm.) film. Thirty cubic centimeters of 35 per cent iodopyracet (diodrast®) is now injected through the no. 18 gage needle connected to the catheter. The injection is done as fast as possible for the first 25 cc.; at the end of this portion of the injection an exposure (with the use of the Potter-Bucky diaphragm and of soft tissue technic) is made, the injection being continued slowly while the film cassette is changed for a second (stereoscopic) exposure. The second exposure is made at the moment the entire amount of dye has been injected. The first part of the injection takes from ten to fifteen seconds; changing the film and the second exposure require about the same length of time. The tourniquets are now removed, and the catheter is withdrawn far enough to leave only a length of 4 to 5 cm. in the lumen of the vein. The proximal ligature is tied taut with one knot around the catheter, and the leg is turned into full internal rotation. The position of the tube is changed to cover the lower third of the thigh and the upper three fourths of the leg. A tourniquet previously put in readiness around the lower leg 8 to 10 cm. above the site of incision is now tied and two stereoscopic exposures are made, the course of injection being the same as just described. The catheter is flushed in with 100 cc. of isotonic sodium chloride solution and withdrawn while the proximal ligature is kept taut and then tied square. The incision is washed out with saline solution and the skin is closed with a single vertical mattress stitch of silk. An elastic bandage is applied from toes to knee.

In every case bilateral phlebograms are taken. The second side is done twenty-four hours after the first one.

Certain precautions must be kept in mind concerning this procedure. Any damage to the sural nerve causes a very annoying and persistent neuralgic pain. Spilling the contrast medium will also result in this complication as well as in a tender induration around the phlebotomy (post-thrombotic limbs are very intolerant of this chemical insult). If

8. We have lately used a special catheter made for intracardiac catheterization. This has some advantages over the ureteral catheter.

9. Tyson, M. D., and Goodlett, W. C.: Venous Pressure in Disorders of the Venous System in the Lower Extremities, Surgery **18**:669 (Dec.) 1945.

any resistance is encountered in passing the catheter, the catheter should be stopped at the point and injection be made at a lower level than usual; the results will usually still be satisfactory, whereas manipulation of the catheter may break the wall of the vein and permit extravasa-

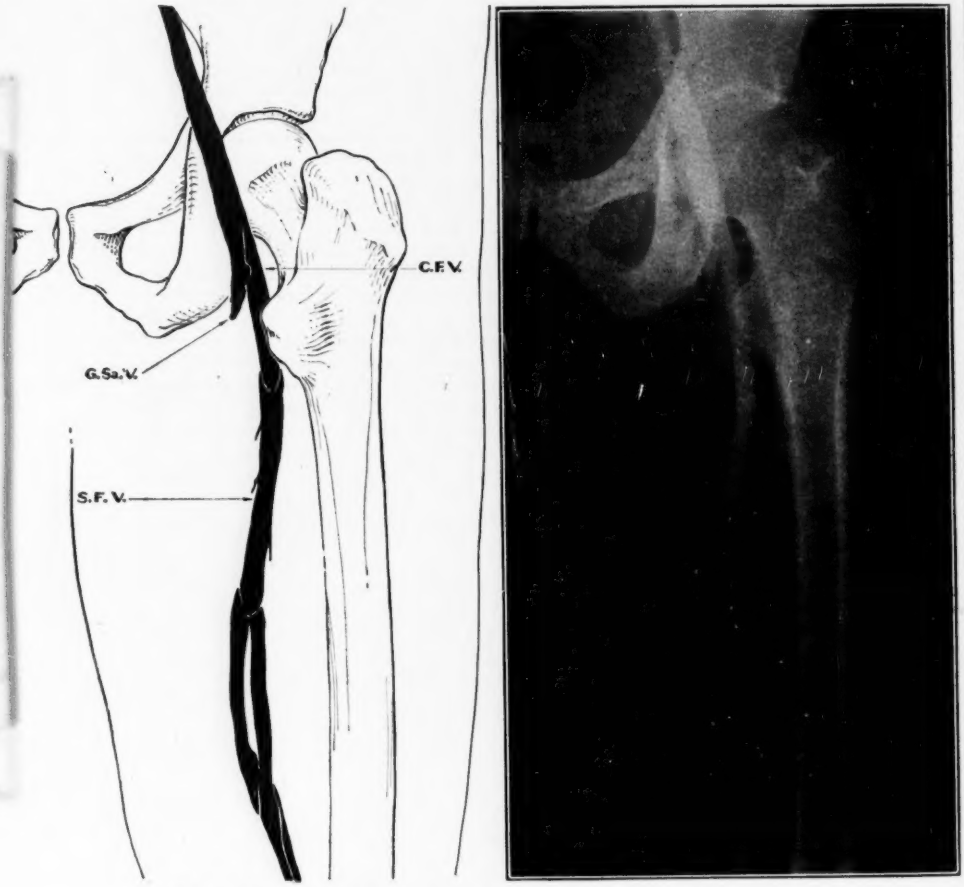

Fig. 3.—Normal phlebogram (posteroanterior) of the right femoral system. The lower superficial femoral vein is bifid. This figure should be compared with figure 5, which represents the opposite limb of this patient. *C.F.V.* indicates the common femoral vein; *G.Sa.V.*, the greater saphenous vein; *S.F.V.*, the superficial femoral veien.

tion of the medium. If one attempts to pass the catheter above the popliteal crease without fluoroscopic control, it may run through a large

communicating branch, which is fairly constant, into the greater saphenous vein and completely spoil the result. Phlebography done in this manner is not always an ambulatory procedure. Patients with no residuals in the leg can continue with their work, but most others should be hospitalized.

Iodopyracet is a safe preparation, but serious reactions may occasionally occur with its use. Each patient should have an intraoral and intravenous test dose at least an hour before administration. Although the amount used by us is large (60 cc. for each side), the excretion of the drug is rapid. In the early cases we followed the course of excretion by K.U.B. (kidney-ureter-bladder) plates and determina-

TABLE 18.—*Results of Phlebography*

	Number of Limbs	Number of Cases	Number of Phlebograms
Totals	..	31	46
Technics of phlebography			
Miscellaneous	..	8	19
Successful results	..	0	0
Catheterization of lesser saphenous vein	..	23	46
Successful results	37	..	40
Unsuccessful results	..	..	6
Findings on phlebograms			
Thigh	37	..	..
Thrombosis of superficial femoral vein above ligature	0	..	..
Thrombosis of superficial femoral vein below ligature	21*	..	..
Recanalization of superficial femoral vein below ligature	7	..	..
Recanalization of superficial femoral vein across ligature	0	..	..
Thrombosis of popliteal vein	12	..	..
Recanalization of popliteal vein	6	..	..
Thrombosis of deep femoral vein	0	..	..
Leg	37	..	..
Incomplete filling of deep veins	15	..	..
Filling with mottling	14	..	..

* There was clinical involvement of the calf in 11 limbs and of the thigh in 5; clinical involvement was not present in 5.

tions of iodine in the urine. In patients with normal renal and hepatic function the renal pelves are not visualized after four hours and the organic iodides disappear from the urine in twelve hours. As an added precaution, our patients had, besides routine physical and laboratory checks, screening tests of renal and hepatic function whenever there was a suspicion of impairment.

We saw no serious reaction in any of the cases. (A few patients were rejected because of positive sensitivity reactions.) In the earlier cases minor wound complications were fairly common (6 cases), but later these were entirely eliminated. Of 46 phlebograms, all but 6 gave adequate visualization for our purposes. The causes of failure were extravasation of the dye (1 case), extensive varicosities (1 case) and inadvertent catheterization of the greater saphenous vein (4 cases).

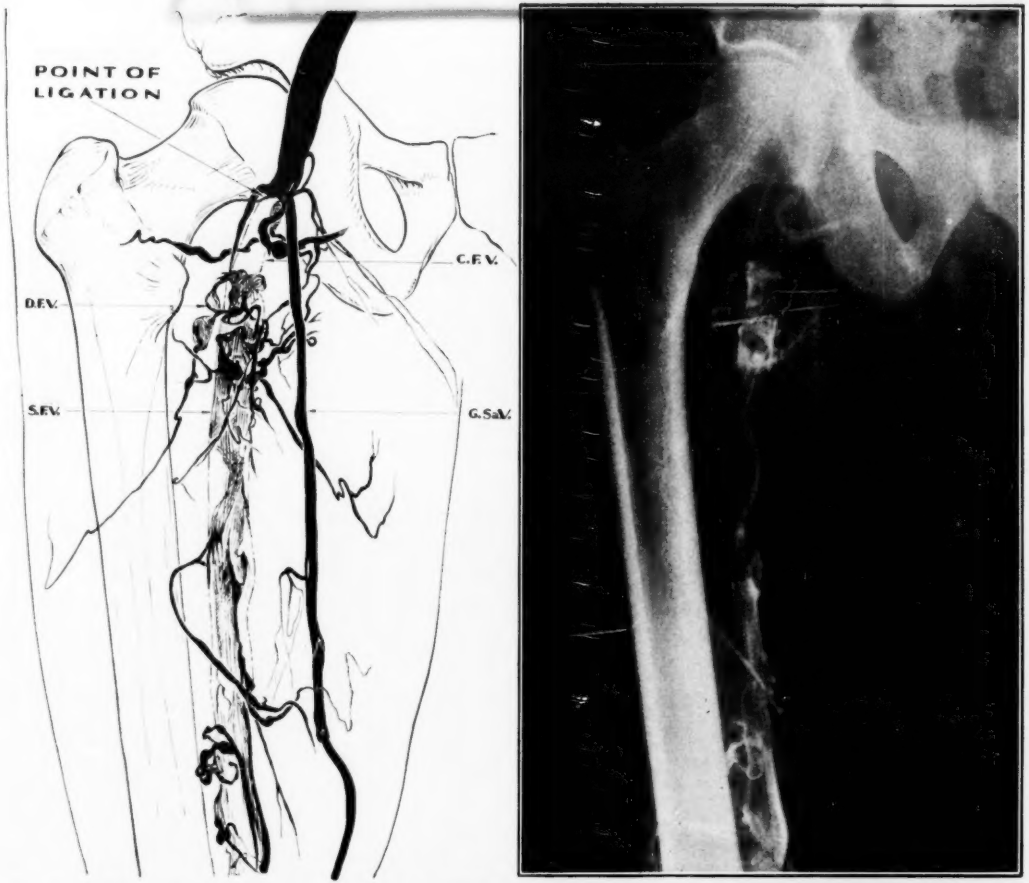

Fig. 4.—Phlebogram of the left femoral system twenty-four hours after ligation of the left common femoral vein for post-operative phlebothrombosis. There was strong clinical evidence of involvement of the calf but no clinical sign of thrombosis above the popliteal vein. The phlebogram shows massive thrombosis of the superficial femoral vein. Only the earliest, narrow and scanty radicals of the collaterals to develop later can be seen. The main drainage channel of the limb at this time is the greater saphenous veins. *D.F.V.* indicates the deep femoral vein; other abbreviations are as in the foregoing figures.

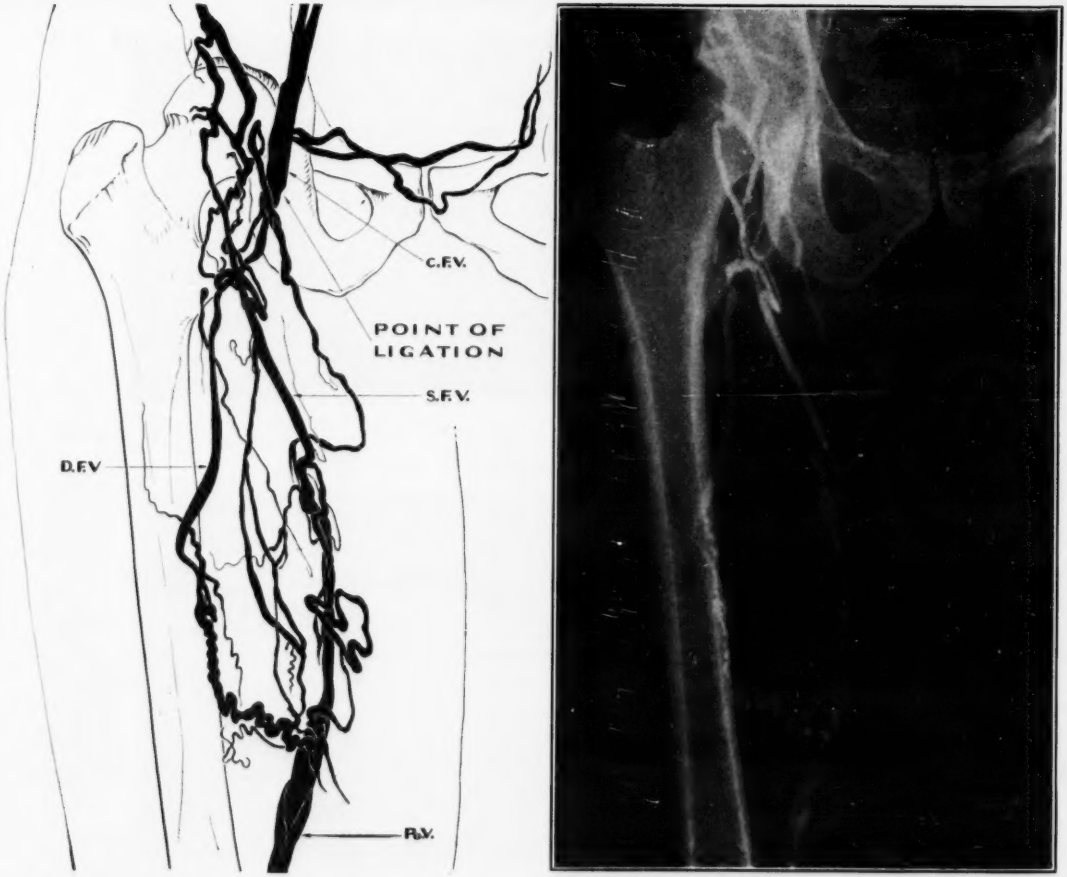

Fig. 5.—Phlebogram of the left femoral venous system thirty-six months after ligation of the left common femoral vein for phlebothrombosis (same patient as in figure 3). The superficial femoral vein has recanalized. *Po.V.* indicates the popliteal vein.

(The technical difficulty created by large and numerous varices can sometimes be obviated by applying an elastic bandage.)

Only 2 patients were rejected for phlebography on account of the post-thrombotic changes in the legs.

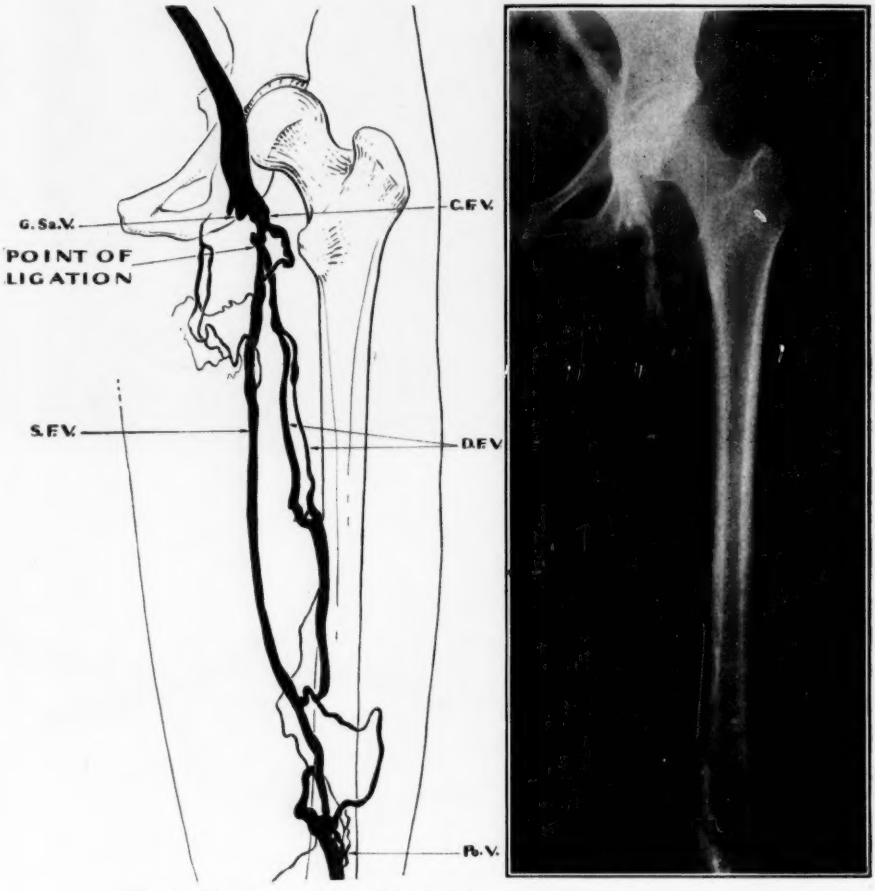

Fig. 6.—Phlebogram of the right femoral venous system twenty-two months after ligation of the superficial femoral vein for phlebothrombosis. The superficial femoral vein has remained patent and is probably functional by way of short collaterals around the point of ligation.

It must be stressed that this method is not proposed as a diagnostic procedure in acute phlebothrombosis. We do not believe that phle-

bography is necessary or helpful in establishing such a diagnosis. The method may, however, have usefulness as a differential diagnostic aid in cases of chronic swelling of the leg.

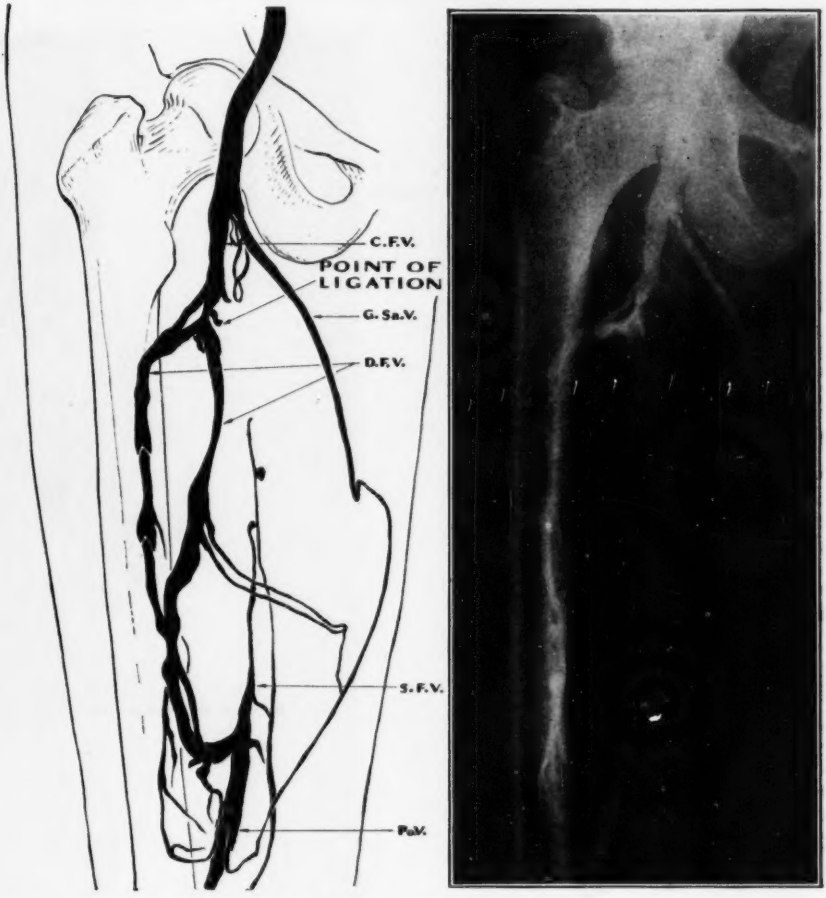

Fig. 7.—Phlebogram of the left femoral venous system forty-two months after ligation of the superficial femoral vein for phlebothrombosis. The superficial femoral vein has become thrombosed and shows partial but ineffectual recanalization. The deep femoral vein is the main drainage channel. The greater saphenous vein shows filling through a communicating branch.

As shown in table 18, we obtained phlebograms in 31 cases of vein ligation. In all but 2 cases the phlebograms were bilateral; in some

cases more than 1 phlebogram was taken on a side for special purposes or because of the failure of the first one. The 46 phlebograms on 37 limbs that form the subject of our further comments were all obtained with the catheterization technic.

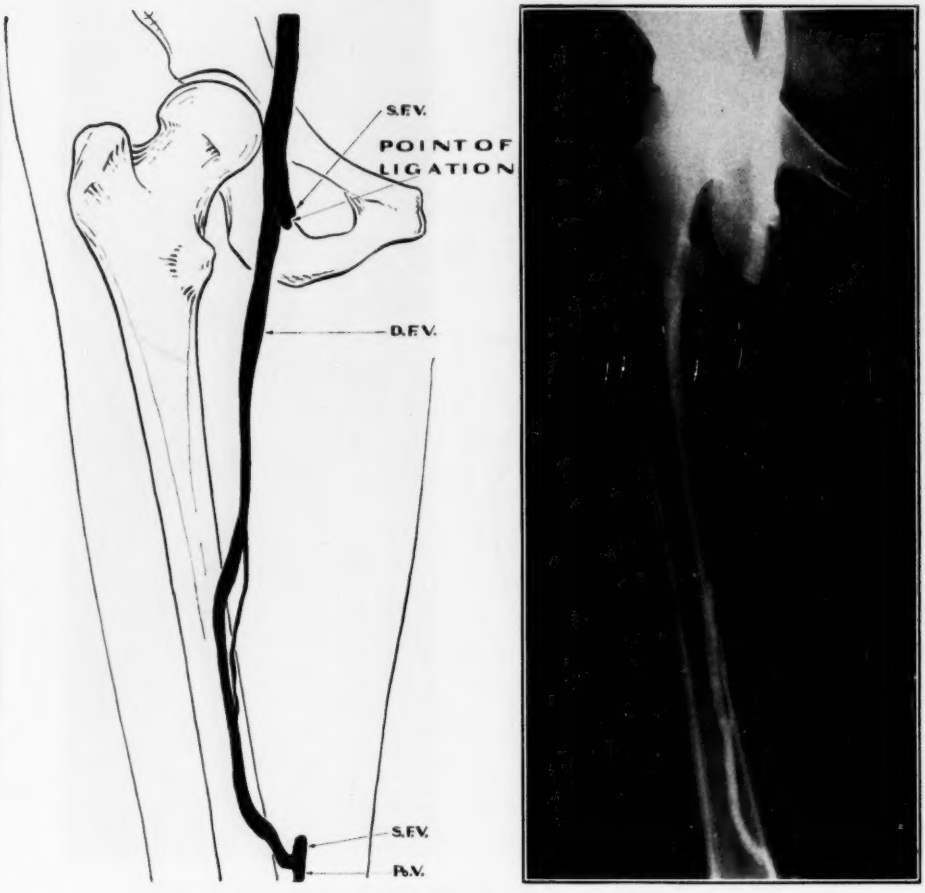

Fig. 8.—Phlebogram of the left femoral venous system eighteen months after ligation of the superficial femoral vein for phlebothrombosis. The superficial femoral vein has been almost completely obliterated by thrombosis. The deep femoral vein is the only draining pathway; its communication with the popliteal vein before ligation must have been direct and very ample.

Phlebographic Observations.—Any interpretation of phlebograms must be prefaced by a remark of caution. The evidence of thrombosis

in a phlebogram is negative—a failure of a vein or a segment of vein to fill with the contrast medium. Even if the technic is reliable and the clinical evidence supports the roentgenographic pattern, a given filling defect may be due to causes other than a clot in the lumen of

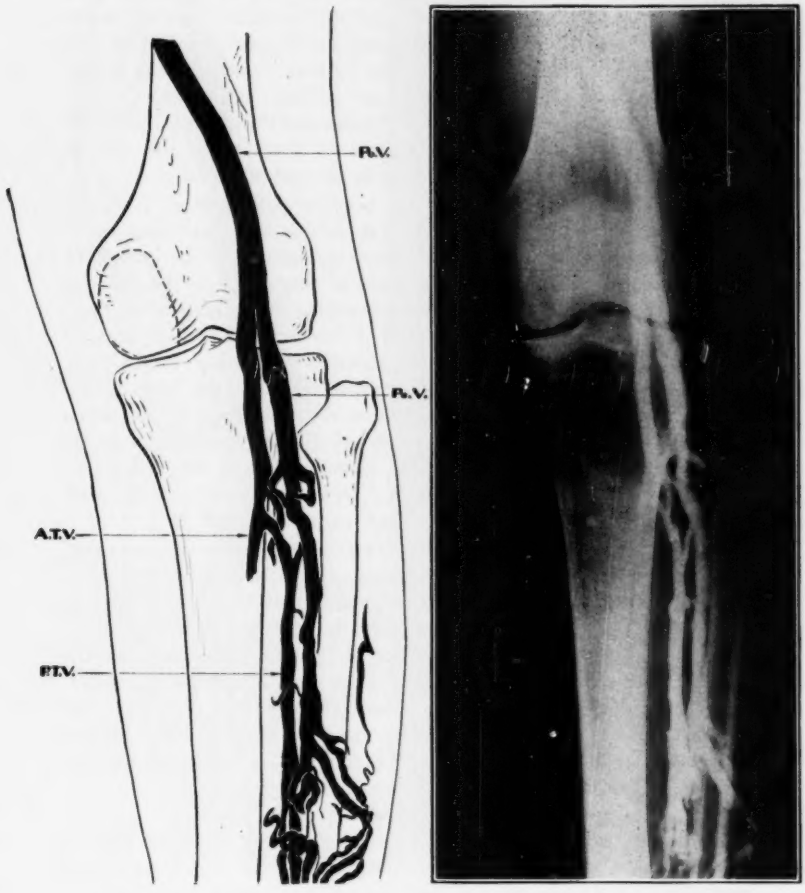

Fig. 9.—Normal phlebogram of the right leg and lower part of the thigh. The anterior tibial vein is not filled sufficiently to allow its visualization through the superimposed tibia. The superficial communications of the peroneal vein are unusually rich and large.

the vein. The dye follows the path of least resistance, and anatomic variations will occasionally lead it away from channels that may be

functionally open. In many situations, therefore, interpretation of a pattern may be a matter of opinion.

The aim of our inquiry in the phlebographic investigation was, as stated before, to follow, as far as possible, the changes in the process of thrombosis in the involved vein from the time of ligation for an indeterminate length of time. The ideal way to achieve this aim would be to obtain serial phlebograms on a number of patients in chronologic order and to correlate the findings case by case. Such a study is now under way, but its practical obstacles are serious. At present we have data only on the different ages of the evolution of thrombosis in different persons (the interval between the time of ligation and the time of phlebography ranging from one day to fifty-seven months).

In attempting to reconstruct the process of thrombosis from the phlebographic evidence of its phases at various time intervals and in different subjects, we selected the following features to be looked for and be compared: presence or absence of thrombosis in the common femoral or superficial femoral veins (according to the level of ligation) below and above the ligature; presence of thrombosis in the deep femoral and popliteal veins; occurrence of recanalization in any one of these veins; presence of thrombosis and recanalization in the veins of the leg; role of the greater saphenous vein in the drainage of the leg when the deep veins are involved; presence and adequacy of collaterals (in the surgical and not in the anatomic sense), including the presence of valves, in both the thigh and the leg. The important observations with respect to these questions are also summarized in table 18.

In the thigh there were two observations of interest that recurred with great constancy: There was no instance of thrombosis in the deep femoral vein after ligation of the superficial femoral vein, and the ligated superficial femoral and common femoral veins never showed evidence of thrombus formation above the site of ligature. The fact that the deep femoral vein remained always patent after ligation of the superficial femoral vein is of great importance from the fact that the vessel (as will be seen) is the most useful collateral pathway after ligation in a large proportion of cases. The complete absence of extension above the ligature in the surgically interrupted venous trunks is significant since many surgeons have feared that such an extension may be a common event; the fact that a spread of the clot above the ligation does not take place is a strong confirmation of the soundness of the procedure of ligation.

The thrombosis of the superficial femoral vein after ligation of that vein in a considerable proportion of the cases that had had no clinical evidence of involvement of the thigh (or any involvement at all) was a surprising observation. This fact would tend to support the assumption that ligation in itself may precipitate clotting in the superficial

femoral trunk. The anatomic circumstance that the superficial femoral vein often receives few tributaries from the level of its junction with the deep femoral vein to the lower third of the thigh seems to predispose

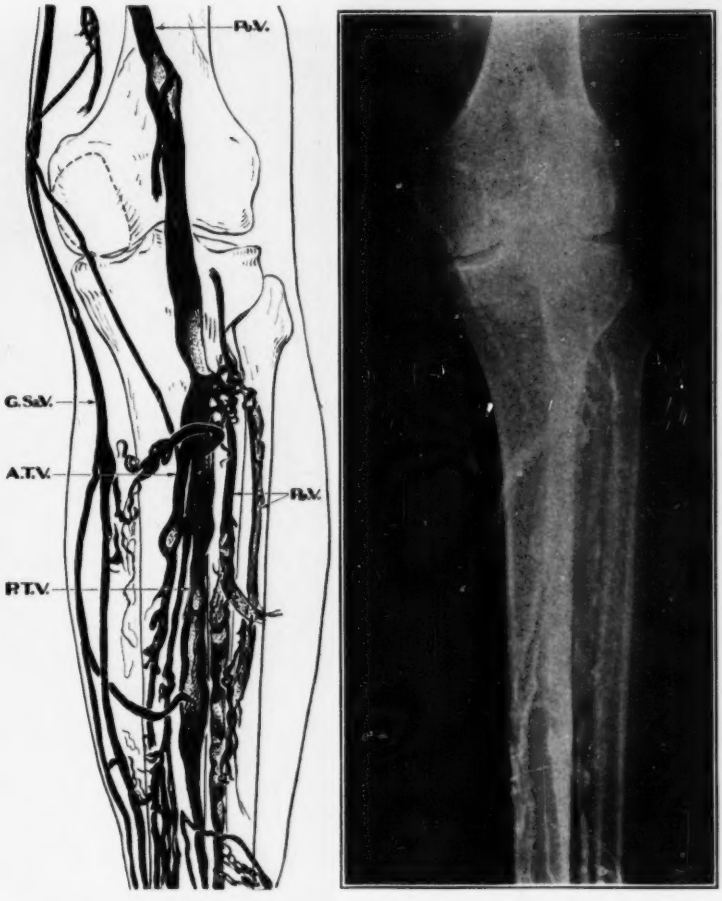

Fig. 10.—Phlebogram of the right leg and lower part of the thigh eighteen hours after ligation of the superficial femoral vein for phlebothrombosis (same case as figure 4.). There is moderately advanced thrombosis of all the deep veins of the leg and of the popliteal vein.

this vein to thrombosis after ligation, since when this vessel is interrupted below the level of the deep femoral vein its trunk is turned into a

practically stagnant channel as far down as the lower end of Hunter's canal. Interestingly, in 7 instances it was exactly this segment that had been closed off by thrombosis. Recanalization when it takes place is rudimentary and probably nonfunctional (valveless) according to phlebo-

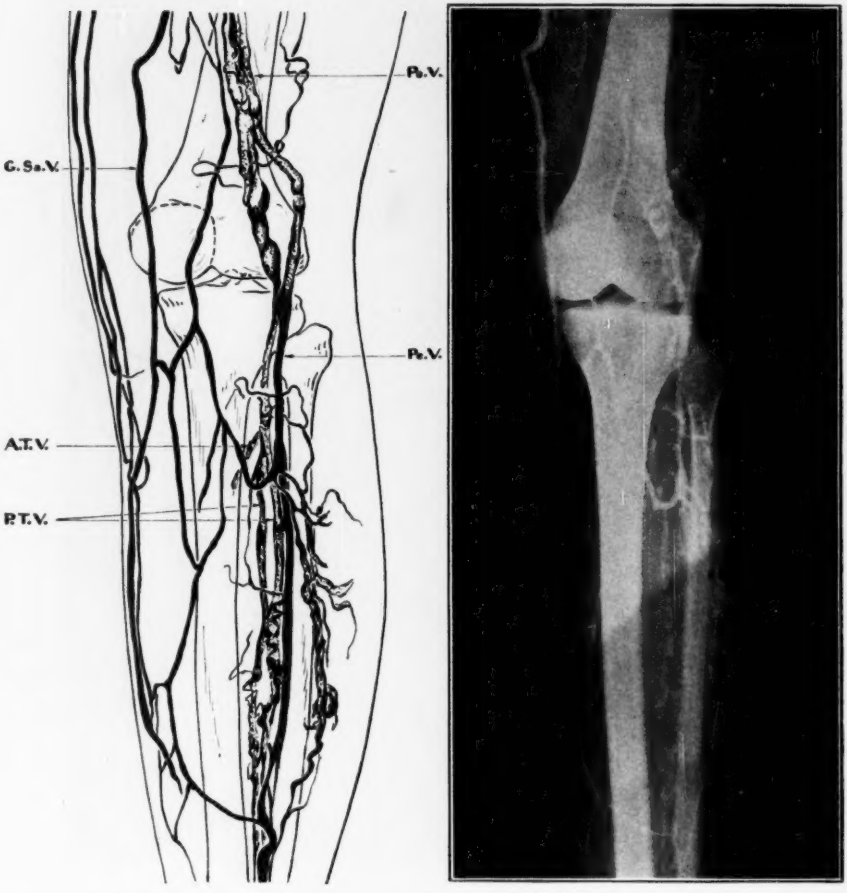

Fig. 11.—Phlebogram of the right leg and lower part of the thigh forty-eight hours after ligation of the superficial femoral vein for phlebothrombosis. The thrombosis is much more advanced than in figure 10. Part of the peroneal vein is curiously spared. Note here, as in figure 10, the heavy filling of the greater saphenous system, on which the main burden of drainage falls.

graphic evidence. There was no example of recanalization of the venous trunk across the point of ligature.

The importance of the deep femoral vein in the formation of collateral circulation is shown by the fact that in every instance of thrombosis of the superficial femoral vein it appears to have taken over the

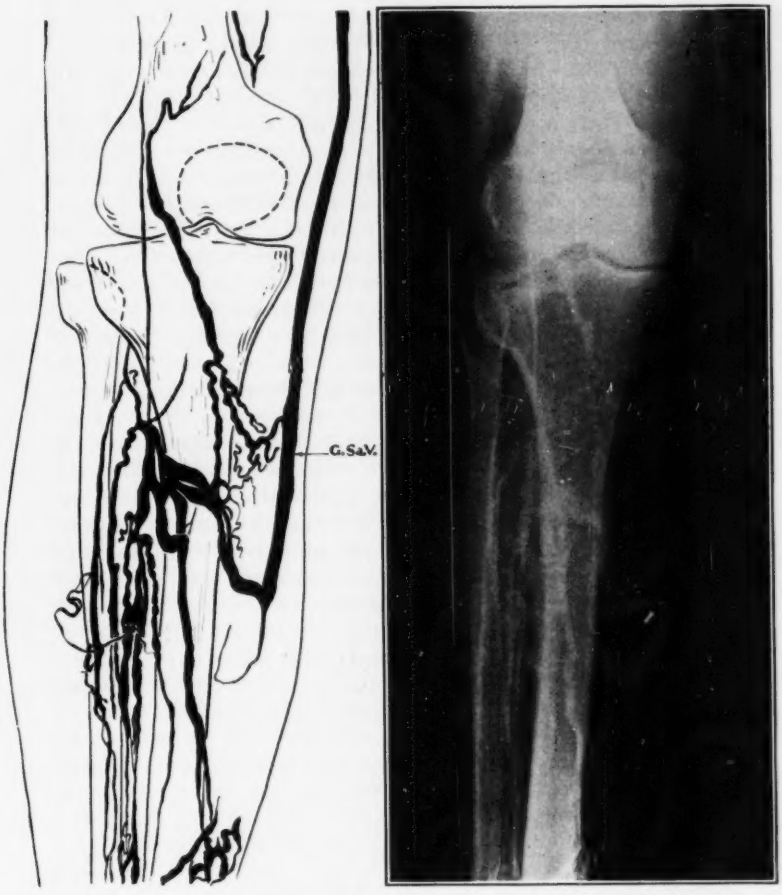

Fig. 12.—Phlebogram of the left leg and lower part of the thigh thirty-nine months after ligation of the superficial femoral vein for phlebothrombosis. The normal pattern of the deep veins of the leg is replaced by an irregular configuration of venous channels, some of which show mottling. The popliteal vein does not fill. The venous return of the leg is, from all appearances, almost entirely through the greater saphenous vein.

entire load of venous drainage of the thigh. It practically replaces the superficial femoral vein.

In the thigh the phlebographically demonstrable collateral circulation after ligation is determined by the level of ligation and the extent of the thrombotic process. Three definite patterns were noted. 1. In the only case of ligation of the common femoral vein adequately investigated (another such has so far been studied only twenty-four hours postoperatively [fig. 4]) three collateral circuits had developed (fig. 5). An inferior circuit was formed for communication between the deep femoral and superficial femoral veins (which partially recanalized); a medial superior circuit appeared to connect the superficial femoral with the common femoral and thence with the obturator and internal pudendal veins; a lateral superior circuit was evident between the deep femoral and inferior gluteal veins. 2. The second collateral pattern is a simple one; it is established when the superficial femoral vein is ligated but remains open. In such cases the important new pathways are those joining together deep and superficial femoral venous trunks in the lower part of the thigh (fig. 6). The third pattern comes about when the superficial femoral vein is thrombosed after it has been ligated. Regardless of the state of recanalization of the superficial femoral vein, the main collateral branches in this instance develop between the deep femoral and the popliteal vein (figs. 7 and 8). As in the former pattern, collaterals of lesser importance may appear also between the common femoral and superficial femoral veins around the site of ligation.

The interpretation of the changes in phlebograms of the leg is less reliable (figs. 9, 10, 11 and 12). The factors that may cause ambiguity, mentioned in an earlier paragraph, hold particularly true here. The rich superficial network of veins may both obscure the configuration and interfere with the filling of deep veins (which are often difficult to see owing to the osseous structures). It can be stated with fair certainty, however, that recanalization in these veins is very common and complete. Only 3 definite instances of marked defects of filling were noted in 26 limbs that had been operated on three months or more before. Evidences of irregular filling were present in 14 cases. Since valves in the deep veins of the legs are hard to demonstrate even in normal phlebograms, it is difficult to make inferences as to the functional state of a phlebographically recanalized leg vein. The collateral channels in the leg are for the most part superficial; at times the greater saphenous appears to carry almost the entire burden of providing a drainage channel around the knee (fig. 12). The significance of this fact is great in relation to the potential dangers of tying or stripping the greater saphenous vein in cases of old thrombophlebitis.

SUMMARY

The early and late changes that occur in the limbs after surgical vein interruption were investigated by clinical and roentgenographic means in 100 cases with 146 vein operations affecting 150 extremities.

Some of the clinical characteristics of the cases composing the series are summarized. The advanced state of thrombotic disease at the time of ligation in a high proportion of these cases is pointed out. In a clinical follow-up survey the success of vein ligation in the prevention of the embolic complication of thrombosis is evaluated and the effect of the operation on the evolution of the local thrombotic process is analyzed. After a short description of a phlebographic technic by catheterization of the lesser saphenous vein, the roentgenographic findings of 46 phlebograms obtained in 23 cases and involving 37 limbs are presented.

CONCLUSIONS

1. In a relatively small group of cases (100 cases with 146 operations) the therapeutic ligation of one or the other of the main venous trunks draining the lower limbs, carried out under proper indications and in the right manner, has been found highly effective in the prevention of pulmonary embolism. Only 1 nonlethal embolic incident occurred after ligation that could be attributed to the failure of the method.

2. A large proportion (80 per cent) of the patients show the appearance of a new swelling or an aggravation of the existing swelling immediately after ligation. After the first postoperative month (and often earlier) this swelling shows consistent improvement for a year if a few simple precautions in the care of the limb are observed. Eventually the condition of a third of the limb returns to normal, and in the remainder, with very few exceptions (less than 2 per cent of the total), the persistent residual changes are not severe enough to interfere with the pursuit of a normal, gainful life.

3. When the superficial femoral vein is ligated directly distal to its junction with the deep femoral vein, there is strongly suggestive evidence in the phlebograms of the ligated limbs that ligation per se precipitates clotting in the segment of the superficial femoral vein lying directly distal to the ligature. There is no proof, however, that this extension of thrombosis adds in any important degree to the permanent sequelae of the pathologic process.

4. With the same technic of ligation (as mentioned in the preceding paragraph) thrombosis has not been noted in the phlebograms proximal to the ligature or in the deep femoral vein. The freedom from clotting of the deep femoral vein permits the formation of an excellent collateral pathway in practically every case of ligation of the superficial femoral vein.

5. As shown by phlebograms collateral circuits of drainage in the thigh are formed in definite patterns that correspond to anatomic expectations and depend on the level of ligation and the extent of thrombosis;

they appear ample. There was no instance of reopening of the venous lumen across the site of ligature. Recanalization of the thrombosed superficial femoral vein has not been seen to have a useful role in the hemodynamic readjustment after ligation.

6. Phlebograms disclose that the deep veins of the leg undergo recanalization in a great proportion of cases. However, restitution of effective venous drainage is in such cases, too, often dependent on the collateral channels which in the majority of instances appear to be superficial (mainly the greater saphenous vein and its tributaries).

Dr. Howard P. Doub and the members of his staff, particularly Mr. Carl Anderson, cooperated in obtaining the phlebograms described in this study.

INTRAVASCULAR AGGLUTINATION (SLUDGED BLOOD), VASCULAR STASIS AND SEDIMENTATION RATE OF THE BLOOD IN TRAUMA

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AND
R. C. HARRISON, M.D.
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IT IS WELL known that drawn blood does not possess the same properties as circulating blood. With the knowledge that blood usually undergoes certain changes as soon as it comes into contact with any material that is not normally a part of the vascular tree, it would appear natural to make observations concerning its physiologic reactions while it is passing unmolested through the vascular bed. To achieve this end not only must one maintain the physiologic state of the tissues in question but microscopic examination requires illumination and the source of light must not be a source of heat or the observations become invalid.

Since the discovery of circulation in 1629 by William Harvey, it is interesting to note how little attention has been paid to the microscopic study of circulation in the living tissues. Special technics and careful manipulation of tissues are required. Methods used in this study are similar to those used by Melvin Knisely [1] and his workers, who have pioneered this field in America. As will be observed in the historical survey to follow, the phenomenon of red cell agglutination has been studied principally in relationship to disease and infection. Only recently has Knisely associated this phenomenon with trauma, and he has coined the term "sludge" to describe the vascular changes which he observed.

The following presentation is a study of both the area of local trauma and the vascular bed remote from the traumatized area. Heat, cold, tourniquet and crush injuries were used. The phenomenon of intravascular agglutination of erythrocytes has been observed in association

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Knisely, M. H.: An Improved Quartz Rod for Living Tissue Illumination, Anat. Rec. **71**:503-508 (Aug.) 1938.

with these forms of trauma, and an attempt has been made to correlate that which is transpiring as a vital changing process with knowledge of suspension stability of the blood and the present concepts of pathology. The fate of these agglutinated clumps of red cells and the possible role of the liver in this regard have been studied.

It was soon evident in this work that descriptions, still photographs, microscopic sections and diagrams were inadequate to record and demonstrate the progressive changes that occur in the vascular bed. Accordingly, colored motion pictures were taken. Altered dimensions of structures and changes in rate of vascular processes were thus preserved as a permanent record.

HISTORICAL SURVEY

From time immemorial, the most favored remedy for nearly all illnesses was blood letting. Usually the evacuated blood differed from healthy blood in that the blood "cake" settled out more quickly, leaving a buffy coat behind. The suspension stability of the blood had been altered in the diseased state. Thus Hippocrates' humoral theory of disease was evolved.

After the discovery of capillaries and erythrocytes by Malpighi, attention was turned to the microscopic changes in the vascular bed. In Boerhaave's "Aphorisms"[2] (1709) it is stated in the description of inflammation that the pathologic process which is the root of many evils consists in stagnation of the blood in the capillaries, whether due to narrowing of the latter through outward influences, mechanical or chemical, or because the blood has become more thickly flowing.

John Hunter[3] in 1786 described pathologic blood thus:

> In all inflammatory dispositions in the solids whether universal or local, the blood has an increased disposition to separate into its component parts, the red globules becoming less uniformly diffuse and their attraction to one another becomes stronger, so that blood when out of the vessels soon becomes cloudy or muddy and dusky in its color, and when spreading over any surface it appears mottled, the red blood attracting itself and forming spots of red.

Cohnheim's[4] lectures on general pathology (1877) drew attention to the changes in erythrocytes in his study of inflammation. The presence of vessels packed with immobile masses of red cells was referred to as "stasis," which he believed due to blood coagulation. Most workers since have believed that this phenomenon was simply due to leakage of plasma, thus leaving the erythrocytes stranded in

2. Boerhaave: Aphorismi de cognoscendis et curandis morbis; 1709; German Translation, Berlin, 1763, p. 146.

3. Hunter, J.: Works of John Hunter, F.R.S. edited by J. S. Palmer: Longmans, Rees, Orme Green & Longmans, London, 1835, vol. 1, p. 235.

4. Cohnheim, J.: The Circulation, in Cohnheim's Lectures on General Pathology, London, New Sydenham Society, 1889, vol. 1.

the lumen of the vessel. Von Recklinghausen, quoted by Tannenberg,[5] differentiated stasis from simple cessation of flow, in that in the latter the red cells remain quite discrete, being suspended in the plasma.

Workers who followed inferred that reconstitution of flow in an area of stasis would always be in the form of discrete cells. Thus the theory of agglutination of red cells in stasis was relegated to the background.

Hüter,[6] in 1786, described the microscopic picture of the nictitating membrane in health and disease. Following the experimental production of septicemias and wound infections in dogs, he found circulating clumps of red cells in the capillaries of the nictitating membrane. These clumps often produced capillary stasis intermittently and then were swept once again into the circulation.

Studies of eclampsia by Schmorl,[7] in 1893, showed hepatic thrombi to be present in the finest branches of the portal system. In 1902 Flexner [8] reported intravascular agglutination of red cells in the region of many infected tissues, as shown by pathologic sections.

Normal circulation was again described by Arey [9] in 1918. He emphasized the fact that red cells remained quite discrete in normal vascular flow, exhibiting no tendency to stick together or even to show rouleau formation.

Correlation of sedimentation rate of the blood with the nature of the flow in the retinal vessels, was attempted by Ploman [10] in 1920. He found that with the compression of the central artery in perfect health the microscopic picture was one of smooth flow. In contrast, people with elevated sedimentation rate showed flowing clumps of erythrocytes.

The great works of Robin Fähraeus,[11] the first of which appeared in 1921, attracted the attention of the whole world to erythrocyte

5. Tannenberg, J., and Fischer-Wasels, B.: Handbuch der normalen und pathologischen Physiologie, 1927, vol. 7, p. 1496.

6. Hüter, C.: Die febrilen Störungen des Blutkreislaufs, mikroskopisch beobachtet an der Palpebra tertia septisch und pyämisch inficirter Warmblüter, Centralbl. f. med. Wissenschaft. **14**:505-510, 1876; Die cheilo-angioskopie, eine neue Untersuchungs-methode zur physiologischen und pathologischen Zwecken, ibid. **17**:225-27 and 241-45, 1879.

7. Schmorl: Untersuchungen über Puerperal-Eklampsie, Leipzig, 1893, p. 15.

8. Flexner, S.: On Thrombi Composed of Agglutinated Red Blood Corpuscles, J. M. Research **8**:316-321, 1902.

9. Arey, L. B.: Observations on the Shape of the Erythroplastid in the Wing of the Bat, Anat. Rec. **14**:135-139, 1918.

10. Ploman, M. O.: Demonstration ophthalmoscopique des variation de stabilité dans la suspension des globule rouges, Ann. d'ocul **52**:569-580, 1920.

11. Fähraeus, R.: (*a*) The Suspension Stability of the Blood, Acta med. Scandinav. **55**:1-228, 1921; (*b*) The Suspension Stability of the Blood, Physiol. Rev. **9**:241-274 (April) 1929.

agglutination. The suspension stability of the blood was thus established as a physiologic phenomenon. Increase in the sedimentation rate of erythrocytes was found to be due to an increased tendency of the cells to form aggregates. He demonstrated a high correlation between the sedimentation rate of erythrocytes and the clumping tendency of circulating erythrocytes in the human nail bed. Experimental injections of hydrophylic colloids, such as gelatin, produced a simultaneous elevation of the sedimentation rate and intravascular agglutination of circulating red cells, as seen in the mesentery of the guinea pig.

The European school recognized the importance of stasis in the inflammatory reaction especially as shown by Ricker [12] and Kreyberg,[13] but it was Tannenberg [5] who, in 1927, contributed an important addition to the theory of vascular stasis. He felt that there was something more than a passive accumulation of red cells. There seemed to be a decreased suspension stability of the blood, with resulting agglutination of red cells into a red homogeneous column, in which individual red cells were not detectable (microscopically in vivo).

Many investigators have since demonstrated the relationship between agglutinated circulating erythrocytes and disease, including Freedlander and Lenhart [14] in 1922, Ruedemann [15] in 1933 and Müller [16] in 1937. Youngner and Nungester,[17] in 1944, showed that type III pneumococcus polysaccharide produced generalized intravascular agglutination in vivo.

The term "sludged blood" was used by Knisely and his co-workers as a comprehensive term to describe abnormal blood flow associated with pathologic states. The name was suggested by the slow uneven flow which may be seen in the general circulation or in areas of tissues exposed to local trauma. Sludge also refers to the agglutinated clumps themselves, and in his article he described several types of sludge according to the size and friability of the masses. The complete blockage of vessels, which has been called vascular stasis in the past, is described as thrombosis by Knisely.

12. Ricker, G.: Pathologie als Naturwissenschaft, Berlin, Julius Springer, 1924.

13. Kreyberg, L., and Rotnes, L.: Acta path. et microbiol. Scandinav. **11**:162, 1932.

14. Freedlander, S. O., and Lenhart, C. H.: Clinical Observation on the Capillary Circulation, Arch. Int. Med. **29**:12-32 (Jan.) 1922.

15. Ruedemann, A. D.: Conjunctival Vessels, J. A. M. A. **101**:1477-1481 (Nov. 4) 1933.

16. Müller, O.: Die feinsten Blutgefässe des Menschen in gesund und kranken Tagen, Stuttgart, 1937-1938.

17. Youngner, J. S., and Nungester, W. J.: The Effect of Type III Pneumococcus, Polysaccharide and Gelatin on the Circulation and Sedimentation Rate of Erythrocytes in Mice, J. Infect. Dis. **74**:247-253 (May-June) 1944.

Knisely and his associates[18] first reported in 1941 intravascular agglutination in the living malaria-infected monkey, and they developed the concept of intravascular agglutination and its relationship to disease and trauma[19] and suggested that the circulating clumps might be a cause of general fluid loss in the body in such conditions as traumatic shock.[20] They also suggested the existence of abnormal phagocytosis of the red cells by the reticuloendothelial system in pathologic states.[21]

METHODS

Two principal methods have been used, one by transillumination and the other by reflected lighting of tissues. In the former, light is conveyed from a 500 watt bulb along a fused quartz rod. The tip of the rod is angulated upward to conduct the beam of light through the overlying tissues. This allows examination of tissues in relatively inaccessible sites. Heat is removed by a water cell filter interposed between the light and the rod. The terminal 6 inches (15 cm.) of the rod is tubular and conveys Ringer's solution, which emerges at the tip and bathes the under surface of the structure being examined. This absorbs most of the remaining heat in the rod.

Mammalian Ringer solution with 1 per cent ash-free gelatin, as suggested by Chambers and Zweifach,[22] was heated in a thermostatically controlled water bath, and, besides passing through the quartz rod tip, it was directed to allow a continuous flow over the upper surface of the structure, thus maintaining an isotonic and isothermic environment at all times. This continuous flow readily absorbed the small amount of heat which is inevitably produced when light strikes tissue, and it rigidly maintained body temperature plus or minus 1 degree C.

Several adjustable holders have been constructed to support the structures and to minimize movement from respiration and arteriolar pulsation. These factors have loomed most important in cinephotomicrography.

The second method of examination entails oblique illumination from a source of light attached to the microscope. This small focusing lamp was

18. Knisely, M. H.; Stratman-Thomas, W. K., and Eliot, T. S.: Observations on Circulating Blood in the Small Vessels of the Internal Organs in Living Macacus Rhesus Infected with Malarial Parasites, Anat. Rec. **79**:90, 1941.

19. Knisely, M. H., and Bloch, E. H.: Microscopic Observations of Intravascular Agglutination of Red Cells and Consequent Sludging of the Blood in Human Diseases, Anat. Rec. **82**:426 (March) 1942. Knisely, M. H.; Bloch, E. H.; Eliot, T. S., and Warner, L.: Sludged Blood, Science **106**:431 (Nov. 7) 1947. Brooks, H. F.; Dragstedt, L. R.; Warner, L., and Knisely, M. H.: The Sequence of Circulating Changes Following Severe Thermal Burns, Anat. Rec. **100**:644 (April) 1948.

20. Knisely, M. H.; Eliot, T. S., and Bloch, E. H.: Sludged Blood in Traumatic Shock: I. Microscopic Observations of the Precipitation and Agglutination of Blood Flowing Through the Vessels in Crushed Tissues, Arch. Surg. **51**:220-236 (Nov.-Dec.) 1945.

21. Knisely, M. H.; Bloch, E. H., and Warner, L.: Selective Phagocytosis: I. Det Kongelige Danske Videnskabernes Selskab, Copenhagen, Biologiski Skrifter, 1948, vol. 4, no. 7.

22. Chambers, R., and Zweifach, B. W.: Topography and Function of the Mesenteric Capillary Circulation, Am. J. Anat. **75**:173 (Sept.) 1944.

fitted with a heat-absorbing filter and connected to a transformer and rheostat. With experience the light could be adjusted to produce sufficient illumination, without undue heat or discomfort to a conscious patient. This method was used in the study of human subjects and larger animals.

Both binocular and monocular microscopes were used, with dry and water immersion lenses, allowing a magnification range of 7 to 400 diameters. With oblique illumination the binocular wide field microscope was attached to a swing arm mounting. Caliber of the vessel was determined by a micrometer scale mounted into the ocular. Cinema recordings were made by a Kodak

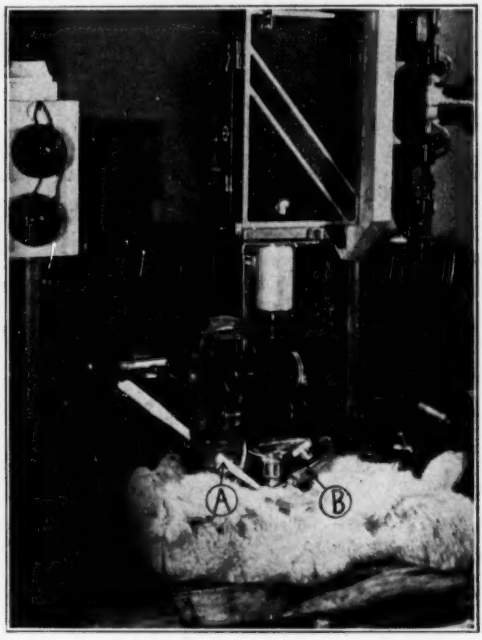

Fig. 1.—Quartz rod transillumination technic. *A*, quartz rod conducting light to tissue; *B*, insulated tube carrying Ringer's solution.

Special® camera mounted conveniently over the microscope. A still camera was similarly mounted.

Warm-blooded animals and human subjects were chosen for the study. Although cold-blooded animals, such as the frog, with erythrocytes 20 microns in diameter, are easier subjects to observe, the difference in constituent elements of the blood made them less desirable. The following animals were examined: 60 human subjects, 88 rabbits, 50 dogs, 10 guinea pigs, 7 mice and 12 rats.

The omentum, bowel mesentery, liver, nictitating membrane, scleral conjunctiva and iris vessels were the areas used for study. It was thus possible to

correlate findings in the different parts of the vascular tree of the same animal. To observe the omentum or mesentery, the animal was carefully opened through the linea alba, sharp scissors being used to minimize hemorrhage and trauma and thus preserve the normal circulation. Organs were lightly handled by fingers or dull hooks moistened with Ringer's solution and placed on a plastic ring under which the quartz rod could be adjusted while they remained constantly bathed in isothermic Ringer's solution. The nictitating membrane was examined by carefully insinuating the dull tip of the quartz rod between the sclera and membrane. The retinal vessels were studied in the rat only, in which the whole eyeball was

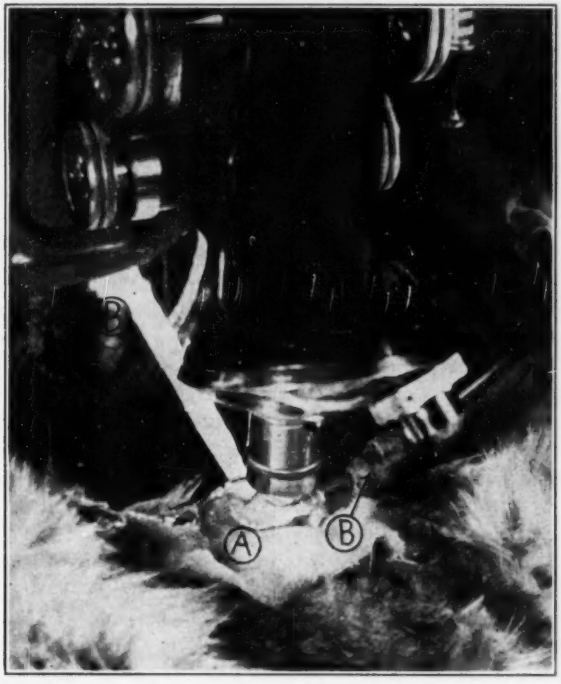

Fig. 2.—Close-up view of transillumination technic. *A*, plastic holder with omentum in place; *B*, tubes conducting saline solution.

transilluminated by the quartz rod. The scleral conjunctiva was studied by reflected light, with manual retraction of the lids. Conjunctivitis or other infections of the eye had to be ruled out.

Knisely's observation that barbiturates did not induce any recognizable agglutination of the cells in many hundreds of animals was confirmed, and this type of anesthesia was used throughout. The human sclera could be examined in the fully conscious patient quite satisfactorily. At all times minimal amounts of anesthetic were used to insure adequate respiration and adequate cardiac function.

Local Trauma.—Animals were examined for the presence of clumping or stasis before each experiment (usually in an eye), and only sludge-free animals were used. Local trauma was studied as applied to the omentum and mesentery. Cold was applied in the form of 20 cc. of Ringer's solution at 3 C., ejected from a syringe, as well as solid carbon dioxide in direct contact with the tissues for one to two minutes. To study the effect of heat, Ringer's solution at various temperatures up to 80 C. was applied. Direct trauma involved injury to the mesentery, bowel or omentum by manual manipulation for periods up to ten seconds with fingers moistened with saline solution or a more localized type of injury from pressure by a blunt probe. As far as possible the same microscopic field was visualized and photographed before and after trauma.

General Systemic Effect.—In this phase of the work the lower extremities of sludge-free healthy anesthetized animals were clipped, exposed to burns, crushing injury or prolonged arterial tourniquet and the effect observed in the vascular tree remote from the area traumatized. Standard 6 per cent burns from boiling water were produced in the extremities after the method of Drinker. Fifteen per cent flame burns were used to produce uniform erythema. Crushing injuries were produced under light pentobarbital sodium (nembutal®) anesthesia by 500 rapid light blows with a rubber mallet, avoiding fractures and internal hemorrhage. Arterial tourniquets were applied high up on the thigh for three to fifteen hours. The degree of trauma has been designated as mild when represented by immersion in boiling water for one and three seconds, and hammer injuries. Severe trauma included exposure to boiling water for five to thirty seconds (rabbits and dogs).

OBSERVATIONS

1. *Normal Circulation.*—The technic of observing tissue by transilluminated light was developed to the point that the abdominal viscera could be observed continuously in a lightly anesthetized animal for periods up to four hours, during which time normal circulation appeared to be maintained. The addition of 1 per cent gelatin to mammalian Ringer solution [22] was found necessary to prevent petechial hemorrhages and evidence of edema after prolonged observation.

The vascular bed differed in minor respects in the various areas examined. Arterioles and venules could be recognized by their size, rate and direction of flow, thickness of wall, pulsations and whether the branches were subdividing or rejoining the main vessel. In the omentum and mesentery, the arteriole terminus, or metarteriole, continued as a thoroughfare channel (Chambers and Zweifach [22]) which, in turn, drained directly into a venule. Here the flow was rapid, and numerous capillaries left each channel to anastomose and reenter at its venular end. There was variation in the length of capillaries, and their diameters ranged from 6 to 15 microns. No evidence of capillary contractility in the mammal has been observed. With experience, a rhythmic variation in diameter, suggesting alternate vasoconstriction and dilation, could be observed in the metarterioles. This has been called "vasomotion" by Chambers and Zweifach. Arteriovenous shunts

were commonly seen as short muscular vessels connecting arteriole and venule.

The flow under normal conditions in all vessels was rapid and smooth. Normal rate in arterioles and venules was indicated by the inability to see individual red cells. In these vessels longitudinal streaks were observed and interpreted as evidence of laminar flow,[23] which denotes the presence of concentric cell layers moving more rapidly near the center of the vessel. A clear area of plasma occupied the periphery. White blood cells glided or rolled freely along as described by the Clarks[24] and were observed occupying the periphery of the stream.

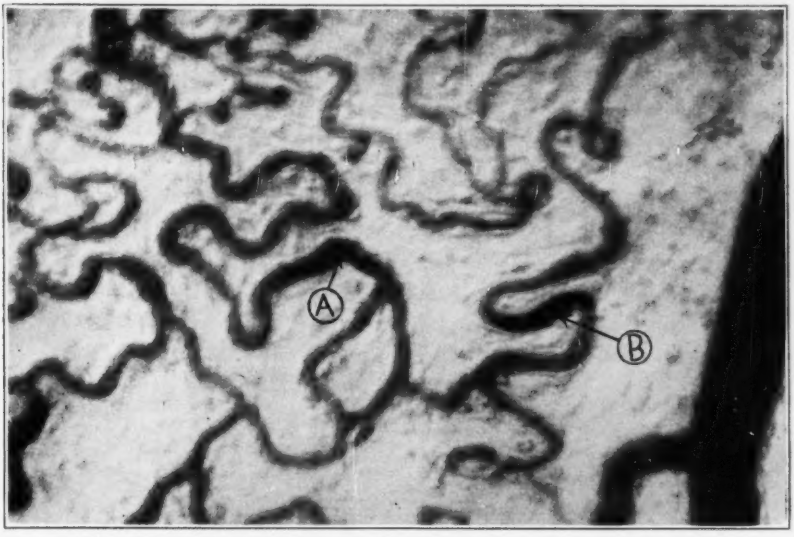

Fig. 3.—Normal circulation of capillary bed (slowed by partial occlusion of arterial flow for the photograph at one-fiftieth second exposure); capillaries 10 to 15 microns in diameter; × 220. *A*, blurred streak of circulating discrete cells; *B*, vessel walls.

The smaller capillaries allowed red cells to flow smoothly in single file, demonstrating what Knisely has aptly termed "a perpetual bottle neck in the circulatory system." The rate of flow appeared to be slower in the longer capillaries. The red cells appeared to remain

23. Krogh, A.: The Anatomy and Physiology of Capillaries, New Haven, Yale University Press, 1929, p. 5.

24. Clark, E. R., and Clark, E. L.: Observations on Changes in the Blood Vascular Endothelium in the Living Animal, Am. J. Anat. **57**:385 (Nov.) 1935.

discrete, with no tendency toward clumping or rouleau formation. Knisely inferred from this fact that the erythrocytes normally repel one another.

2. *Local Trauma.*—In this phase of the study, the area of the vascular bed being traumatized was under continuous microscopic observation before, during and after injury. Experiments were conducted on 21 animals.

In all forms of trauma studied the vascular response was similar. With moderate changes in environmental temperature, such as inadequate control of the temperature of the Ringer solution, representing

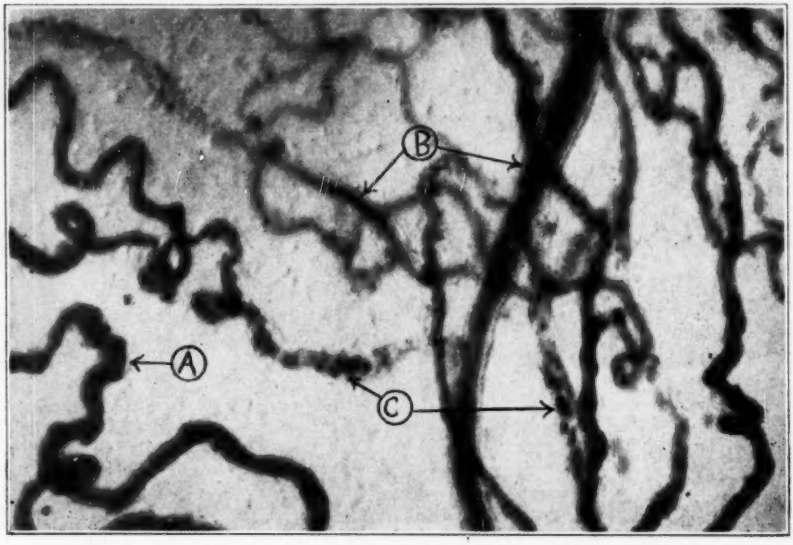

Fig. 4.—Local trauma; × 150. *A*, static capillaries—dark red homogeneous columns of blood; *B*, flowing capillaries and venules—peripheral layer of plasma well shown; *C*, clumped erythrocytes at junction of static and flowing blood.

a minimal degree of trauma, slowing of the rate of flow occurred. This caused a granular appearance in the larger venules and arteries. This might progress to a very slow porridge-like flow, probably due partly to hemoconcentration and partly to red cell cohesion. Perivascular tissues showed evidence of varying amounts of edema. Many capillaries became static. White cells began to adhere momentarily to the injured endothelium and eventually became fixed in spite of continued flow in the vessel. This occurred earliest in the venous end of the capillaries. Diapedesis was observed, and these cells were

noted to pass into the tissues, as described by the Clarks.[24] In severer trauma the picture is predominantly one of rapid or instantaneous appearance of stasis.

Heat in the form of Ringer's solution at 80 C. produced stasis—that is, widespread immediate cessation of flow with apparent agglutination of erythroyctes into homogeneous dark red columns. With the continuation of the physiologic environment, resolution was observed in arterioles and venules and in capillaries at the periphery of the burned area. The first evidence of resolution was seen with the appearance of pulsation in some of the blocked arterioles, synchronous with the heart beat, and minutes later these vessels were cleared of their obstruction and blood was flowing. The capillary bed remained static until the conclusion of the experiment and for the most part was short circuited by arteriovenous shunts.

The application of Ringer's solution at 3 C. produced a similar picture, although resolution occurred in all vessels, including capillaries, within a few seconds.

Solid carbon dioxide caused an immediate cessation of flow which was resumed as soon as thawing occurred. After five to twenty seconds gradual slowing of the blood stream occurred, which progressed to stasis. Partial resolution occurred during the next two hours, with some capillaries remaining in a condition of stasis at the conclusion of the experiment. This reaction is similar to that observed by Quintanilla, Krusen and Essex,[25] who applied solid carbon dioxide to a Clarke window inserted into a rabbit's ear.

After crushing injuries to tissues, the same picture of widespread vascular stasis appeared. The manual manipulation or probing was very mild, such as could be produced during a gentle abdominal operation. The degree and rate of resumption of flow varied with the severity and duration of trauma.

Blalock,[26] in his studies of shock, reported: "The oxygen content of the blood from the femoral vein of a traumatized leg was high, while that of blood from the opposite extremity and head was low." He attributed the reduction in arteriovenous oxygen difference in the injured leg to "an accumulation of blood in the area traumatized, and unusual diminution in the amount of blood in other areas." We feel that such findings would be expected. The vascular stasis produced by trauma opens up arteriovenous shunts and allows the blood to pass

25. Quintanilla, R.; Krusen, F. H., and Essex, H. E.: Studies on Frost-Bite with Special Reference to Treatment and Effect on Minute Blood Vessels, Am. J. Physiol. **194**:149 (April) 1947.

26. Blalock, A., and Bradburn, H.: Distribution of the Blood in Shock, Arch. Surg. **20**:27-38 (Jan.) 1930.

into the venous circulation, without the usual reduction in oxygen content.

Resolution of Stasis.—At various intervals following trauma, in the vessels which had been blocked with columns of red cells flow was resumed. Careful observation of this process of resolution of stasis showed that in many instances at least, in which it was possible that one could observe the vessel at the moment of resolution, the red cells were no longer discrete but left the area and passed into the general circulation as clumps or aggregates of apparently agglutinated cells. Some of these agglutinated clumps contained only a few cells, whereas others, particularly those from larger vessels, were large masses that passed down the vein of exit like an express train. One could often observe the formation of these agglutinated clumps of red cells at a point where a freely moving vein joined one in a condition of stasis, as illustrated in a frame from the motion picture.

The resolution of stasis columns into discrete red cells, which pass as such into the general circulation, has also been observed. What factors determine the mode of resolution of vascular stasis are not known. The length of time that the vascular bed has been static may well be a factor in the production of agglutination.

Thus local trauma produced local stasis, and the breaking up of these static columns was observed. Agglutinated clumps of erythrocytes passed into the general circulation, henceforth to be identified as sludge.

In this study 21 animals were examined for the local effect of trauma. From a previously normal circulation, stasis was produced in each case and with all forms of trauma used.

3. *General Effect of Trauma.*—The presence of circulating clumps of agglutinated red cells has been observed in the general circulation in the past. It has usually been associated with disease states and trauma. This phase of study was devised to correlate by a controlled experiment the exact relationship between the local reaction to injury and general sludging of the vascular tree. Can these agglutinated red cell masses, formed at the site of trauma, be identified in the general circulation?

(*a*) Mild trauma (as described in "Methods") applied to two legs of the animal was not complicated by surgical shock, and the animals were active and ate well when they recovered from the anesthetic. Repeated observations of the conjunctiva and viscera were made, before and after trauma. On observation of the conjunctiva, the vascular bed appeared normal for two to four hours following injury, whereupon the earliest signs of abnormal circulation appeared. Blood

flow through the small vessels, particularly venules, became granular. In some capillaries the flow was in bursts or was intermittent because of partial or temporarily complete obstruction by agglutinated red cell clumps. Longer capillaries showed a series of clumps passing along, not unlike a string of beads. The narrow caliber conjunctival vessels showed early slowing and interesting reversal of the direction of flow.

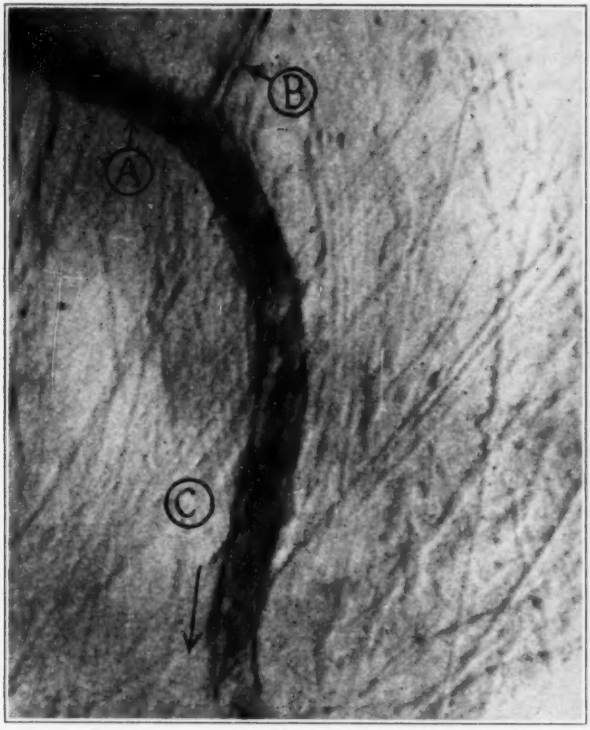

Fig. 5.—Resolution of stasis (frame from motion picture). *A*, static homogeneous column of blood; *B*, arteriovenous shunt in which the blood is rapidly flowing and washing clumps free; *C*, clumps flowing down draining venule into the general circulation.

At twelve and twenty-four hours the generalized effect had progressed so that there were many metarterioles, capillaries and venules which were filled with red cells exhibiting no movement. This condition of stasis appeared to be a result of blockage by the circulating agglutinated masses or sludge.

Circulation in the large vessels was slower and the flowing material appeared granular. The conjunctiva was glistening and edematous, and at the twelve hour interval the surface was irregular, indicating a variation in the degree of edema. Several times elevation of the conjunctiva was observed directly over a capillary which had been suddenly occluded by a circulating clump. These observations were taken as evidence of generalized loss of fluid from the vascular tree, associated with the phenomenon of sludging. To support this concept, it is noted that Moon,[27] using an intravascular vital dye, observed evidence of generalized fluid loss in traumatic shock.

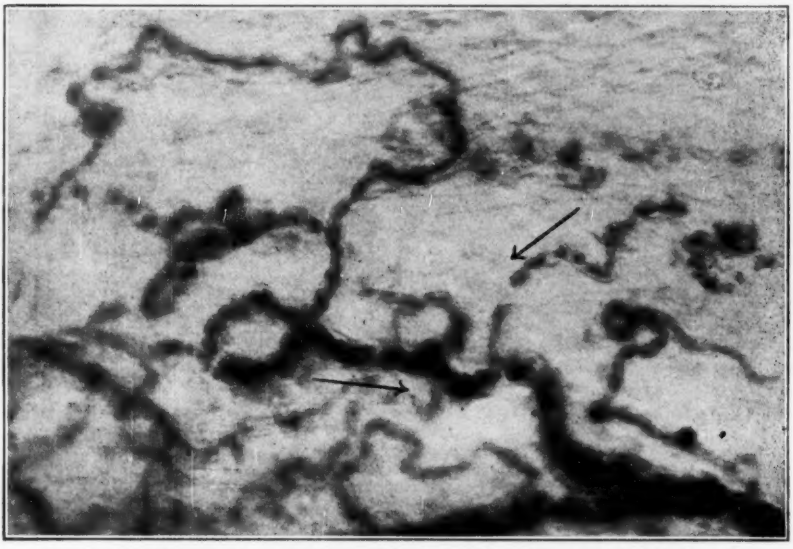

Fig. 6.—General effect of trauma (circulation slowed by partial occlusion of arterial flow for the photograph at one-fiftieth second exposure); × 220. Circulating clumps flowing through capillary bed.

In five to ten days, most of the stasis had resolved, but there was still evidence of occasional agglutinated masses of red cells passing through the capillaries.

At some point in the experiment, the omentum and mesentery were exposed and examined, in order that the changes in them might be correlated with what had occurred in the conjunctiva. Here the thinner tissues permitted much clearer observations, higher magnifica-

27. Moon, V. H.: Shock: Its Dynamics, Occurrence and Management, Philadelphia, Lea & Febiger, 1942, p. 122.

tion and greater detail for photomicrography. The picture was somewhat different from that observed in the conjunctiva. Agglutinated masses were observed producing capillary bursts and intermittent flow, but in this mild trauma little or no stasis developed and the flow was more rapid. This is apparently due to the shorter and wider-calibered capillaries found in the portal system.

(*b*) Severe trauma (described in "Methods") was complicated by some degree of secondary shock with hemoconcentration. Of 20 dogs submitted to ten second burn, hematocrit determinations performed on 8 showed an average rise of 8 points, or 21 per cent increase over initial reading. Continuous recordings of blood pressure were made on 5 of 15 rabbits by means of a cannula in the carotid artery. All these showed a fall in blood pressure within one to two hours. Further details of this work will appear in a future publication dealing with shock.

Similar observations were carried out on the vascular bed remote from the area of trauma. The flow appeared abnormal in five to twenty minutes in all animals studied. The changes progressed with greater rapidity. The predominant feature was slowing, and stasis appeared to develop as a result of progressive slowing. In twelve and twenty-four hours definite circulating clumps could be observed in the slowly flowing blood, but their size and number were not in keeping with the degree of stasis present and suggested that the obstruction to flow had been produced by factors other than embolic blockage. Stasis was observed in both the conjunctiva and the omentum, and, once again, it was more pronounced in the former area. Edema developed in the conjunctiva. The loss of transparency in the omentum suggested the development of edema here.

The presence of general stasis has also been observed by Zweifach and Chambers,[28] while examining the living omentum in tourniquet shock experiments. Moon [27] has observed evidence of visceral capillary stasis in histologic sections taken from experimental shock experiments.

In the present study, the number of animals traumatized and the number in which sludging developed are shown in table 1.

It may be pointed out that in the severe forms of trauma, the slow, porridge-like stream which Knisely described as sludge, effectively camouflaged or made it impossible to determine the presence and size of circulating clumps. In the main, it was felt that clumps were present in all animals.

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28. Chambers, R.; Zweifach, B. W., and Lowenstein, B. E.: The Peripheral Circulation During the Tourniquet Shock Syndrome in the Rat, Ann. Surg. **120**:791-802 (Nov.) 1944.

In sludge-free animals exposed to mild trauma without shock or significant hemoconcentration, agglutinated masses of red cells appeared in the general circulation consistently after injury. The stasis which resulted appeared to be due to blockage of capillaries by circulating clumps, was mild in degree and varied in different regions of the vascular bed.

In severe trauma a similar sequence of events occurred, but it was masked by hemoconcentration and shock, both of which can be major factors in the slowing of the circulation and stasis.

TABLE 1.—*Systemic Effect of Trauma*

Degree of Trauma	Animals		Number Showing Change			
			In Conjunctiva		In Mesentery	
	Dogs, No.	Rabbits, No.	Clumps	Stasis	Clumps	Stasis
A. Mild						
Burns	20	..	20	20	Not seen	
	..	10	10	10	10	0
Hammer blows	..	10	10	10	10	0
B. Severe						
Burns	20	..	20	20	Not seen	
	..	15	15	15	15	15

TABLE 2.—*Survey on 60 Human Subjects*

No. of Subjects	Degree of Agglutination and Stasis			Clinical Symptoms of Disease		
	Nil	Minimal	Moderate	Nil	Mild	Moderate
26	25	1	..	26	..	..
9	..	9	..	..	9	..
23	..	..	23	..	..	23

2 (discarded because of possible conjunctivitis)

4. *Incidence of Agglutination of Red Cells in Human Subjects and Laboratory Animals.*—Examination of the conjunctiva for the presence of agglutination of red cells was made in 60 human subjects in an attempt to confirm Knisely's observations. Medical students, nurses, hospital employees and bed patients were studied.

The results are set forth in table 2. Moderate clinical symptoms included those of patients confined to the hospital with burns or frostbite or convalescing from major operations. Mild clinical symptoms included head colds, sore throats, infected fingers and others.

It is interesting to note that only 1 of 26 apparently healthy subjects showed any degree of intravascular agglutination. Infections of the upper respiratory tract produced some degree of agglutination in almost

every case. There was a rough correlation between the severity of the illness and the degree of the agglutination. Two subjects who showed agglutination with abnormal flow were omitted because of possible conjunctivitis.

All experimental animals were examined initially as they came from the cages. Of a group of 88 rabbits, 49 were normal and 37 showed evidence of fine to moderate clumping, with various degrees of stasis. In one third of the latter, there was some obvious evidence of disease, such as subcutaneous abscesses, nasal discharge or diarrhea. On occasion all animals showed pathologic flow on several consecutive days, suggesting that the presence of a contagious disease among them was responsible for the clumping. In the last two winters it was

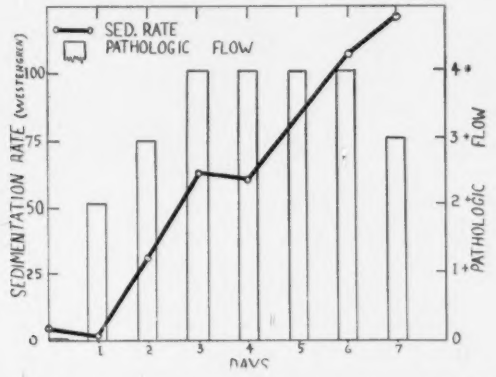

Fig. 7.—Relationship between sedimentation rate and pathologic flow. (Pathologic flow refers to a combined assessment of intravascular agglutination and vascular stasis.) A seven day study of 5 healthy dogs subjected to 6 per cent burn in boiling water for one to two seconds.

found necessary to discontinue work for periods of several weeks, because all the animals showed pathologic circulation.

Dogs from the cages showed a lower incidence of pathologic flow. Of 55 dogs, 39 showed normal circulation and 16 showed agglutination.

5. *Suspension Stability.*—Robin Fähraeus' [11a] work on the relationship between suspension stability, or sedimentation rate, and intravascular agglutination has been confirmed in this study. Routine determinations of sedimentation rate were carried out on 20 dogs, fresh from the cages. Eleven were sludge free, and with 1 exception all had sedimentation rates below 10. Of the 9 showing circulating clumps of red cells, all had sedimentation rates ranging from 10 to 100. The sedimentation rate appeared roughly to parallel the degree of agglutination.

Sedimentation rates were followed on 30 burned dogs. These were selected animals, with normal-appearing circulation and sedimentation rates within normal limits. After the burn, intravascular agglutination of red cells and vascular stasis were observed in all animals within one hour. The sedimentation rate, however, decreased during the first twenty-four hours and then rose to very high levels. Five of these dogs were followed for seven days, and the results are illustrated graphically (fig. 7). This temporary lack of correlation between sedimentation rate and pathologic flow may be attributed to other factors which are already known to influence suspension stability, such as

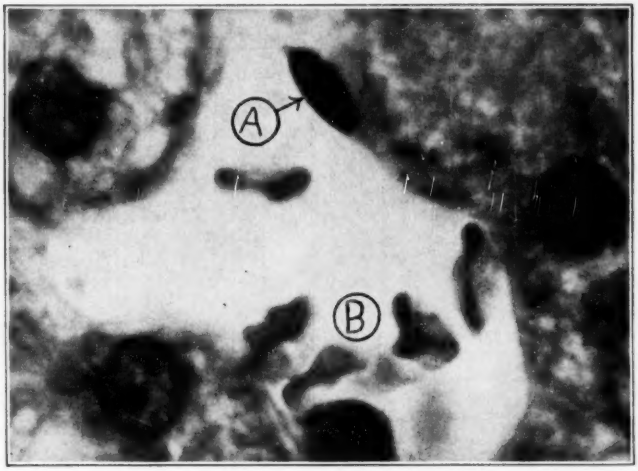

Fig. 8.—Histologic section showing normal liver sinusoid. *A*, Kupffer cell—no phagocytosis; *B*, discrete free red cells. Hematoxylin and eosin; × 2,100.

hemoconcentration, protein content of the plasma or alteration of temperature, hydrogen ion concentration and electrolytes.

6. *Fate of Agglutinated Cells.*—Coincident with the healing of traumatized tissue, the circulation returns to its former state. Whether the blood undergoes deagglutination or whether the clumps are phagocytosed by the reticuloendothelial system we do not know. Whether or not the ingestion of the clumps of red cells represents the fate of all or only some, such a process would serve as a possible explanation of the anemia that follows trauma.

Knisely [21] has observed the ingestion of coated foreign particles by the phagocytes of the liver in living frogs. He has suggested—but

not reported—that Kupffer cells may ingest the agglutinated clumps of red cells, because of a fibrin-like coating similar to that covering the foreign particles. At autopsy of 27 dogs performed twenty-four hours after both severe and mild burn, all showed enlargement and marked engorgement of the liver.

The liver has been transilluminated and observed at intervals in normal rabbits and after burns. A reasonably good view of the sinusoid circulation was obtained and photographed. Immobilized masses of red cells were observed on occasion, and it was reasonable to suspect that they were ingested clumps which had been produced

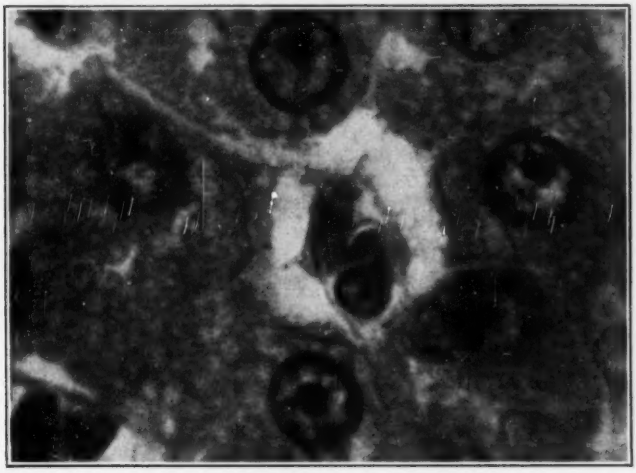

Fig. 9.—Histologic section of liver sinusoid from traumatized animal. Kupffer cell distended, with two red cells in its cytoplasm. Hematoxylin and eosin; × 2,100.

by the burn. Pathologic sections of liver taken at intervals of three hours to eight days following burns were compared with the normal. Hematoxylin and eosin and prussian blue stains showed evidence of phagocytosis of intact red cells in 5 livers from 15 burned animals. A similar study as a control indicated the presence of phagocytosis in 1 liver among those taken from 5 normal animals. These histologic observations were made by Dr. S. Bensley, who was not aware of the nature of the section under examination.

7. *Vascular Stasis.*—This term has been used in the historical outline and throughout our observations to denote complete cessation of flow in vessels as a result of trauma. We have already concluded

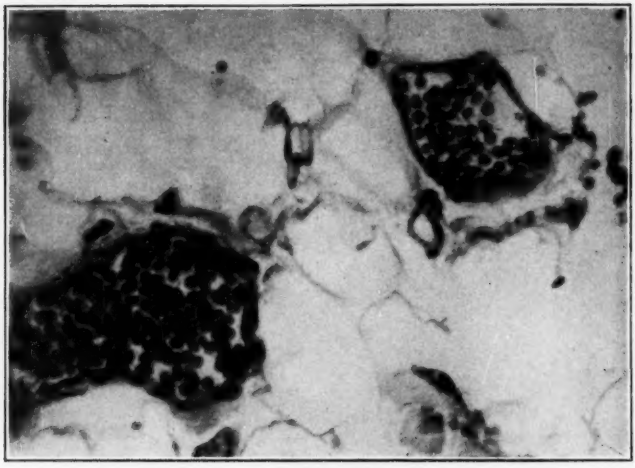

Fig. 10.—Section of normal subcutaneous tissue; discrete red cells in venule. Hematoxylin and eosin; × 440.

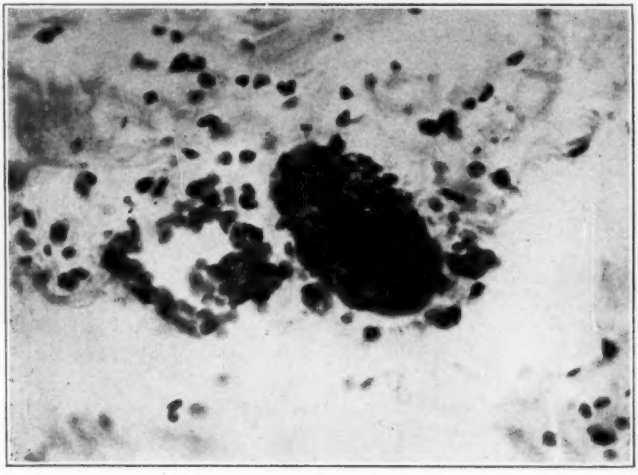

Fig. 11.—Section of subcutaneous tissue after burn to adjacent skin. The red cells are closely packed and probably appeared as a dark red homogeneous mass before fixation of tissue. Hematoxylin and eosin; × 440.

that this invariably takes place and that the extent of the stasis and the time taken for resolution depend on the extent and duration of the injury.

In an attempt to correlate these observations with the pathologic picture, sections were taken of skin and muscle of the burned and hammered extremities of dogs and rabbits studied. These showed the familiar picture of capillaries and larger vessels packed with red cells. Most American pathologists describe this as congestion or hyperemia and incorrectly imply thereby that there is still flow present. It is interesting to note the divergence of opinion that exists between European and American pathologists on this fundamental reaction of tissues. Further confusion is added by the popular American interpretation of the word stasis as meaning slowing of the circulation.

In this study vascular stasis has also been observed in areas remote from the region traumatized. In injury uncomplicated by hemoconcentration or shock, this stasis was considered due to embolic blockage of vessels by agglutinated clumps of red cells. Observations on shocked animals suggested that vascular stasis could be produced by hemoconcentration or slowing of the stream induced by shock. We should therefore like to postulate five important causes of vascular stasis associated with trauma: (1) local reaction to injury, (2) embolic blockage, (3) hemoconcentration, (4) reduced hydrostatic pressure (shock) and (5) vasoconstriction.

It would appear difficult or impossible at the present time definitely to identify vascular stasis on pathologic section. This is no doubt due to the series of dehydrating chemicals to which tissues are exposed before they reach the slide. When photomicrographs of normal skin and that taken twenty-four hours following a burn are compared the latter shows what pathologists have described as congestion. Our studies would indicate that vascular stasis existed in the burned skin, but these slides are difficult to interpret and do not clearly demonstrate the process seen in vivo.

COMMENT

The nonspecific nature of the physiologic processes of intravascular agglutination of erythrocytes and vascular stasis is evident. It is apparently linked with coagulation of blood and influenced by the many changes which occur in the blood's colloid and electrolytic states.

Many obvious questions arise:

1. *What causes vascular stasis in local reactions to injury?*—Is it due entirely to leakage of fluid with silting of red cells, or is there a physical-chemical alteration of the state of the blood which causes local agglutination? We observed evidence of fluid leak, but we

have also sometimes observed the resolution of the stasis column into agglutinated clumps of red cells. In support of the latter theory, we have observed an increased susceptibility to vascular stasis in animals already showing a degree of generalized intravascular agglutination.

2. *Are the agglutinated clumps of red cells formed only in the traumatized area, or is there a chemical alteration in the blood which induces a generalized clumping throughout the vascular tree?*—Agglutinated clumps of red cells have been observed leaving the traumatized area. Whether or not they represent the sole source of clumps following injury is not known. Since reduced suspension stability is a generalized reaction on the part of the blood, one might suspect that both factors are in operation.

3. *Should the term "sludge" be used to denote the presence of agglutinated clumps of red cells slowing the circulation, or should it include the slow porridge-like flow seen with hemoconcentration and shock?*—Knisely has used the term "sludge" to denote all the microscopic circulatory changes following trauma (and disease). He described generalized retardation of flow by agglutinated clumps of red cells with subsequent stasis. He has not clearly indicated that a similar picture, with generalized vascular stasis, can be produced in severe burns or traumatic shock very early and before many agglutinated clumps have entered the circulation. This very early picture appears to be one of low blood pressure and hemoconcentration from loss of fluid at the site of injury. The latter concept will be clarified in a paper to follow.

4. *Is vascular stasis an important cause of tissue anoxia and resultant tissue death following local trauma?* [29]—This question is to be dealt with in a later paper.

5. *Is the process of erythrocyte agglutination a factor in the production of shock?*—It would appear to be a cause of generalized fluid loss following injury and thus could add to the loss of circulating blood volume. It is well known that the fatal volume of local fluid loss from trauma is less than the fatal volume of loss from hemorrhage. This constitutes a possible explanation of the discrepancy.

6. *Is the extension of vascular stasis the origin of red clot formation in phlebothrombosis?*—This would appear to be a natural sequel to stasis, but until there is a means of identifying stasis and thrombosis pathologically it will probably remain unanswered. There is

29. Bigelow, W. G.: The Modern Concept and Treatment of Frost-Bite, Canad. M. A. J. **47**:529-534 (Dec.) 1942. Kreyberg and Rotnes.[18]

very probably an important time factor related to the reversibility of stasis.

7. *Could embolic blockage of kidney cortex by agglutinated red cells be a factor in the production of traumatic anuria, or the "crush" kidney?* —Trueta was interested when it was suggested to him that cortical vessels could become static from embolic blockage by circulating clumps. This type of production of stasis with the opening of arteriovenous shunts, as he described in his work on the "crush" kidney, is typical of the vascular response seen in all tissue studied.

8. *Could phagocytosis of the agglutinated red cells be a cause of secondary anemia following burns?*—This has been already discussed. A further explanation might be that there are diminished erythropoietic properties of the red marrow as a result of the embolic effect of the circulating clumps.

9. *Is the process of erythrocyte agglutination a beneficial reaction in trauma?*—This is an intriguing question and will probably not be answered until the deagglutinating agent has been found. The previous questions suggest that in advanced degrees this is a deleterious process, but it may be found eventually to be beneficial.

These and many other questions which arise are as yet unanswered and indicate the need for further study.

SUMMARY

1. Observations and microscopic cinema recordings were made on the living vascular bed in health and in reaction to trauma. An attempt was made to clarify the meaning of the terms vascular stasis and sludge.

2. The methods of study described made it possible to maintain the living vascular bed in its normal physiologic state for four hours.

3. Normal blood flow was smooth and regular, with no tendency for erythrocytes to agglutinate. There was no vascular stasis, and the sedimentation rate was usually below 10.

4. After local trauma to the area under microscopic observation, there was cessation of flow in the smaller vessels. The red cells became packed into dark red homogeneous masses. This phenomenon has been described as vascular stasis. Resolution of stasis was observed, in which the columns often broke off into the general circulation as circulating clumps.

5. Animals exposed to trauma consistently showed agglutinated clumps of red cells in the general circulation after injury. These clumps appeared to act as emboli and produced stasis in areas remote from the trauma.

6. In trauma followed by shock, hemoconcentration and reduced rate of flow complicated the picture.

7. It was difficult to correlate the picture of stasis seen in vivo with that seen in histologic sections.

8. Possible clinical applications of the phenomenon are discussed.

9. Microscopic cinema recordings have been made in color to demonstrate each phase of the study.

Prof. R. M. Janes, head of the department of surgery, and Mr. Walter Cowan, senior technician, cooperated in this study. Dr. Sylvia Bensley, of the department of histology, interpreted the histologic sections.

Department of Surgery, University of Toronto.

DISCUSSION OF PRECEDING PAPERS

DR. JOHN H. OLWIN, Chicago: I should like to comment very briefly on Dr. Lillie's paper concerning the prevention of pulmonary embolism—that is, regarding the methods for the control of anticoagulants, particularly dicumarol.® I agree that the early use of heparin, before dicumarol® becomes effective, is very important. Dr. Lillie mentioned that in certain instances thrombi developed after the patient had been on anticoagulants. I believe that a certain percentage of these, perhaps a large percentage, is the result of an inadequate control of the anticoagulant effect. Dr. Quick's method, which is used rather universally, does not take into account a large number of variables in the coagulation process and may give a false prothrombin reading as a result of the overactivity or underactivity of one or more of them. On the other hand, the two stage method, which was devised by the group at Iowa City and which is not well enough known, controls these factors and, for the most part, measures only the prothrombin level. In a series of cases which we have followed with the use of the two stage method we have been able to reduce the prothrombin to a therapeutic level and maintain it there rather uniformly, which we have been unable to do with the Quick test run in parallel with the two stage test. The latter method has two particular advantages: First, it is much safer because it does not allow the patient's prothrombin to drop to a hazardous bleeding level without the knowledge of the person who is controlling the therapy. Second, if bleeding does occur, it is usually slight and because the patient's prothrombin level is not far below the bleeding threshold it is often unnecessary to use heroic measures to bring the prothrombin back to a safe level, and hence the therapeutic effect is not disturbed.

If the two stage test is used more universally, I believe that results with anticoagulants will be materially improved.

DR. LOUIS G. HERRMANN, Cincinnati: At the Cincinnati General Hospital the conservative amputation of gangrenous toes has been practiced for over fifteen years. We are entirely in accord with what Dr. Regan has said about the reduction in mortality and loss of limbs in patients with gangrene or localized infection in the joints of the feet. The presence of a gangrenous toe in a diabetic patient is no longer an absolute indication for a supracondylar amputation. It has been our experience, however, that the transmetatarsal type of amputation gives a much better weight-bearing foot than simple removal of the toes, especially when the first metatarsophalangeal joint is destroyed by gangrene or infec-

tion. I want to emphasize the fact that in performance of the operation the tendons must be anchored in their sheaths by transfixed sutures of fine chromic surgical gut before they are cut. Some failures have been due to retraction of these tendons, especially the extensor tendons of the toes, with spread of the infection up the tendon sheaths. Transmetatarsal amputations of this type give good functioning stumps which do not require special prosthesis for normal weight bearing and locomotion. It is important to save as much plantar skin as possible, so that the end of the stump will be partly covered by the thick plantar skin when healing and contraction of the stump takes place. The dorsal part of the end of the stump is usually covered by small split thickness skin grafts after a good granulation tissue base has developed.

Our experience supports the belief and experience of Dr. Regan and his associates that many legs can be saved and made useful again even when one or more toes are gangrenous. Stimulation of the arterial circulation and the use of antibiotics and chemotherapeutic agents have greatly lessened the risks of conservative amputations, even in the face of infection in a diabetic patient.

I should like to ask Dr. Lillie whether it is the policy at the University Hospital suddenly to discontinue use of anticoagulant drugs in the management of venous thrombosis. We have found that there is a sudden rise in the coagulability of the blood when anticoagulants are discontinued abruptly. Some of the so-called recurrences of venous thrombosis after adequate periods of anticoagulant therapy may be due to this peculiar phenomenon. I should advise use of small doses of heparin or dicumarol® for three to four weeks after all signs and symptoms of venous thrombosis have subsided and the patient is normally active again as the best means of preventing sudden recurrence of venous thrombosis.

DR. WALTER W. CARROLL, Chicago: I wish to commend the author of the paper on hernia and should like to bring up merely one point. I also favor early ambulation, but fair evaluation of the vascular complications must include a more complete consideration of the patient's activities prior to hospital admission, as well as of his inactivity as a result of the anesthesia. Of course, patients have been known to rest in bed at home before coming to the hospital. On the other hand, it is equally possible to discover that a patient has been exercising strenuously before entering the hospital, with the possible formation of a spontaneous clot in one of the small veins of a leg. Such patients will confuse the statistics. In addition, when a patient is under spinal anesthesia or general anesthesia for some time (perhaps the anesthesia lasts only two hours, yet the patient lies quietly another four hours in bed) a venous clot may form from such inactivity.

I should like to commend Dr. Coller's representatives on their feeling about anticoagulants. It is obvious that you will find out in a minute or two that I have a deep prejudice, built on enthusiasm perhaps, against femoral ligation and in favor of anticoagulants. Some of the 7 deaths in this series might have been averted if the anticoagulants had been applied routinely to that group. It was interesting to note that there were no deaths in the group receiving anticoagulants.

In reference to Dr. Szilagyi, one might conclude that such a study could arise from a feeling that we have to defend the concept of femoral vein ligation by pointing out the absence of sequelae in the lower leg. Three months is not enough time to use as a measuring stick for follow-up of femoral vein obstruction. Bauer and his group of Swedish clinicians, with one of the best controlled studies on possible phlebitis sequelae, have shown that one to two years follow-up is more complete. In support of the use of anticoagulants in phlebothrombosis, they made the very pertinent point that in the beginning the clot is located in one of the vena comites, distal to the popliteal junction. The reason that the anti-

coagulants do so well is that clotting is prevented in all the other parallel branches and normal collateral return is not mechanically impeded. Not only is it the migration of the clot that we are concerned with but also the sequelae. If the anticoagulants are used, we will tend to keep many venous channels open for the return flow. Femoral vein ligation, of necessity, produces occlusion and obstruction of return flow.

DR. J. SUTTON REGAN, Buffalo: I should like to state that a number of patients who have just the one large toe remaining think that their balance is aided by it. At least it does not seem to impair their walking ability. The big point that I should like to make today is that we have reduced our high amputations from 70 per cent to 18 per cent, and a number of people have useful legs, which formerly would have been amputated.

DR. JOHN H. POWERS, Cooperstown, N. Y.: If I have left with the discussers of my paper the impression that I do not favor early ambulation, I have been grossly at fault. In my opinion, early postoperative activity has everything to recommend it and nothing to condemn it. I wish to impress on this audience, however, that many of the reports in the literature about the decrease to the point of nonexistence of vascular complications among patients who have been permitted early postoperative activity are not in accord with my own experience. I have read papers, as you no doubt have, by surgeons whom many of us know, stating that they have operated on 1,500 patients, 2,000 patients or 10,000 patients with not a single instance of postoperative thrombosis when ambulation has been allowed on the first postoperative day. Gentlemen, that does not happen. Thrombosis in the deep veins of the legs is not only not eradicated by prompt postoperative activity, but the frequency of this complication is unaltered by early ambulation. As for remaining in bed or going on a spree in preparation for operation, I live in a rural area where the patients have no time to stay in bed and no money to spend on bibulous holidays before reporting for hernioplasty. In fact, most of them do their evening chores, enter the hospital the next morning, have their hernias repaired the following day and go home from three or four days to seven or eight days afterward. They are back milking the cows two weeks from the day they were operated on.

DR. R. H. LILLIE, Ann Arbor, Mich.: Certainly we have something to gain from Dr. Olwin's first observation, that our control of the prothrombin levels in patients treated with anticoagulants is far from perfect. We attempted to report here what our experience has been in the past, and that includes the first patients to whom we gave anticoagulants. I believe our complications are being diminished, especially as far as hemorrhage is concerned, and perhaps the thing that is going to help most is a better test to follow the prothrombin levels. However, I should like to say—repeating myself somewhat—that patients' sensitivity to anticoagulants, particularly dicumarol,® is not uniform, and in spite of following the level daily or oftener, two individual patients may have quite different responses to the same dosage, and the level may be quite rapidly changed in one patient by what would be a moderate dose for the other. In regard to the second question, I think we certainly agree that heroic methods are not at all necessary if the prothrombin level falls to what would be considered a dangerous level if allowed to persist. When it is between 10 and 20 per cent, we discontinue further administration of dicumarol,® but this does not necessarily mean that one must resort to massive doses of vitamin K or blood transfusion to bring up the patient's prothrombin concentration. In our experience, when a low level is noted on one determination, dicumarol® is discontinued, and the prothrombin concentration will

usually rise automatically in sufficient time to prevent bleeding. In regard to Dr. Herrmann's question, "Is it policy to discontinue anticoagulants quickly?" I think that he has in mind the raising of prothrombin concentration suddenly. The anticoagulants are discontinued in the usual case of venous thrombosis after a period of ten days. The patient is allowed to regain normal prothrombin concentration, and if he is ready to go home we frequently resort to an amount of vitamin K sufficient to bring the patient's prothrombin concentration to 50 per cent, which we would consider a safe level to allow the patient to leave the hospital if he is not going to take any more dicumarol.

D. D. Emerick Szilagyi, Detroit: Dr. Carroll has stated that we are partial to ligation of veins. I should like to point out that while he, by his own admission, professes prejudice against such ligation, we are definitely not prejudiced against the use of anticoagulants. As to the remark that our statistics are not entirely valid since serious sequelae commonly occur after three or more months of freedom from trouble following ligation, I must say that I am unaware of any account in the literature that would bear out this point. The statistics of Swedish investigators, in particular those of Gunnar Bauer to which Dr. Carroll refers, did not concern postligation cases. They dealt with medical and postoperative thrombophlebitis treated with heparin. The cases with serious sequelae described in these studies were all neglected ones of long standing, and they are in no way comparable to those of our series. Our patients were closely watched, as mentioned in our paper, for periods varying from one month to seven years, and we can say with assurance that if a patient had no sequelae at the end of three months, he had no sequelae at the end of any further period of observation provided he obeyed a few simple rules in the care of the affected limb.

It was not our purpose in our presentation to prove the superiority of one method over another or to establish criteria for the application of either form of treatment. As a matter of fact, the exclusive use of either method is unwise. There are cases in which ligation is the better choice; anticoagulants, now becoming increasingly more popular, must be given preference in other cases. In this series we have limited ourselves to the use of vein interruption mainly for the purpose of evaluating the method in general and to observe its effects on the limb. No doubt, in the future a balance will be struck and the indications for each method will be clearly defined. In the meantime, I think it is a useful undertaking to attempt to find out what one may expect in the evolution of the changes that ligation brings about in the affected limb.

BIOPSY OF DIFFUSE PULMONARY LESIONS

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ALEXANDER J. ANLYAN, M.D.
AND
GEORGE M. CURTIS, M.D.
COLUMBUS, OHIO

DIFFUSE, extensive, bilateral pulmonary lesions producing minimal symptoms and frequently found on routine roentgen examination present a challenging diagnostic problem. They may represent a fibrotic reaction to inhalation or radiation trauma or to infection, both bacterial and fungus; a primary pulmonary neoplasm, or metastatic lesions from asymptomatic primary carcinoma elsewhere. A presumptive diagnosis can occasionally be made on the basis of the history; examination of bronchial fluid, blood and bone marrow; sensitivity studies, or biopsy of peripheral lymph nodes. An absolute diagnosis, however, cannot be made in a large number of patients by these indirect methods. In a series of 50 patients we have been able to diagnose such lesions with certainty by the use of a simple technic of pulmonary biopsy, which in our experience has led to no serious complications and has been of minimal discomfort to the patients.

SURGICAL TECHNIC

In the first 12 cases in which pulmonary biopsy was done, endotracheal anesthesia with pentothal sodium®-curare induction was used; however, because of occasional bronchitis and laryngitis observed in these patients, cyclopropane-oxygen delivered under positive pressure with a face mask is the form of anesthesia now in use. Since the biopsy specimen is taken from the inferior border of a lobe, we have found an anterior incision in the third or fourth intercostal space on the right to be most advantageous, this approach giving access to the inferior margin of the upper, middle and lower lobes.

The surgical procedure is illustrated in figure 1. After routine preparation of the skin with the patient in a supine position an 8 cm. incision is made over the fourth anterior intercostal space, beginning

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From the Department of Research Surgery, the Ohio State University. Aided by a Grant from the Comly Fund for Research of the Ohio State University.

4 cm. from the lateral border of the body of the sternum (fig. 1, *1*). In women the incision is made submammary, and upward retraction of the breast is used to expose the third or fourth intercostal space. After separation of the fibers of the pectoralis major and minor muscles, the intercostal space is exposed and the intercostal muscles cut midway between the margins of the ribs. The blades of a medium-sized Richardson retractor are inserted parallel with the ribs into the incision and when the handles are rotated 90 degrees outward spreading of the ribs occurs, with adequate exposure of the interlobar fissure (fig. 1, *2*).

With slight increase in the intrabronchial pressure by the anesthetist, the lower margins of the upper, middle or lower lobes will herniate

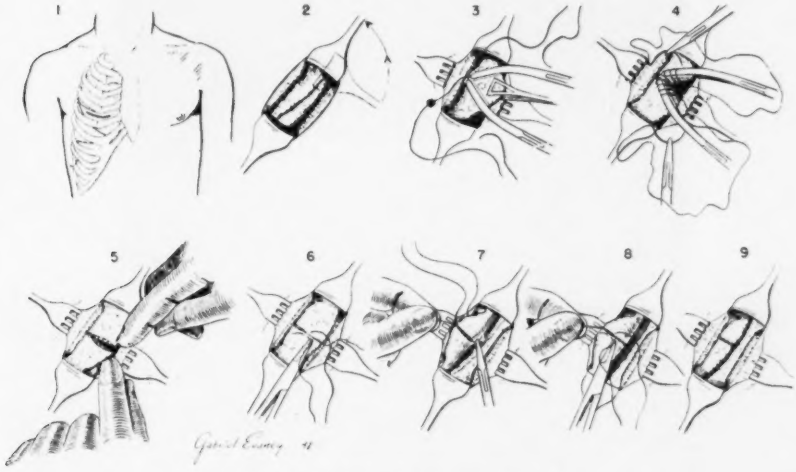

Fig. 1.—Technic of pulmonary biopsy.

through the incision. A small Duval lung clamp is used to grasp the edge of the lobe at the proposed site of the biopsy. A mattress suture of 000 chromic surgical gut with a swaged curved needle at each end is placed at the apex of the biopsy site 2 cm. from the margin of the lung. Two Carmalt hemostats are now applied with the tips approximating the placed mattress suture, isolating a wedge of pulmonary tissue, which is now sectioned and removed (fig. 1, *3*).

The two ends of the suture are now run down as an over and over stitch to the periphery of the lung on each side (fig. 1, *4*). The Carmalt clamps are removed, the suture pulled tight and the two ends tied to bring the cut surfaces together (fig. 1, *5*). One end of the suture is used as a continuous Cushing stitch to appose the visceral pleural

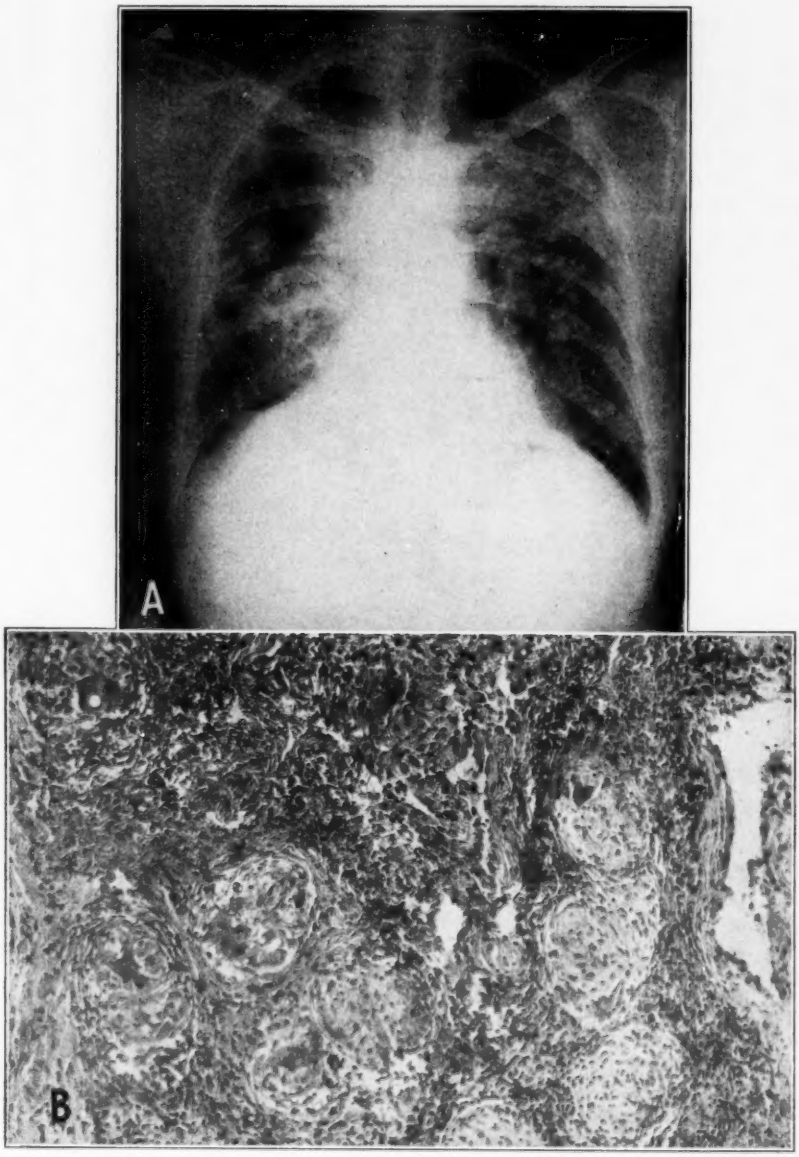

Fig. 2 (case 1).—*A*, roentgenogram, and *B*, photomicrograph of Boeck's sarcoid.

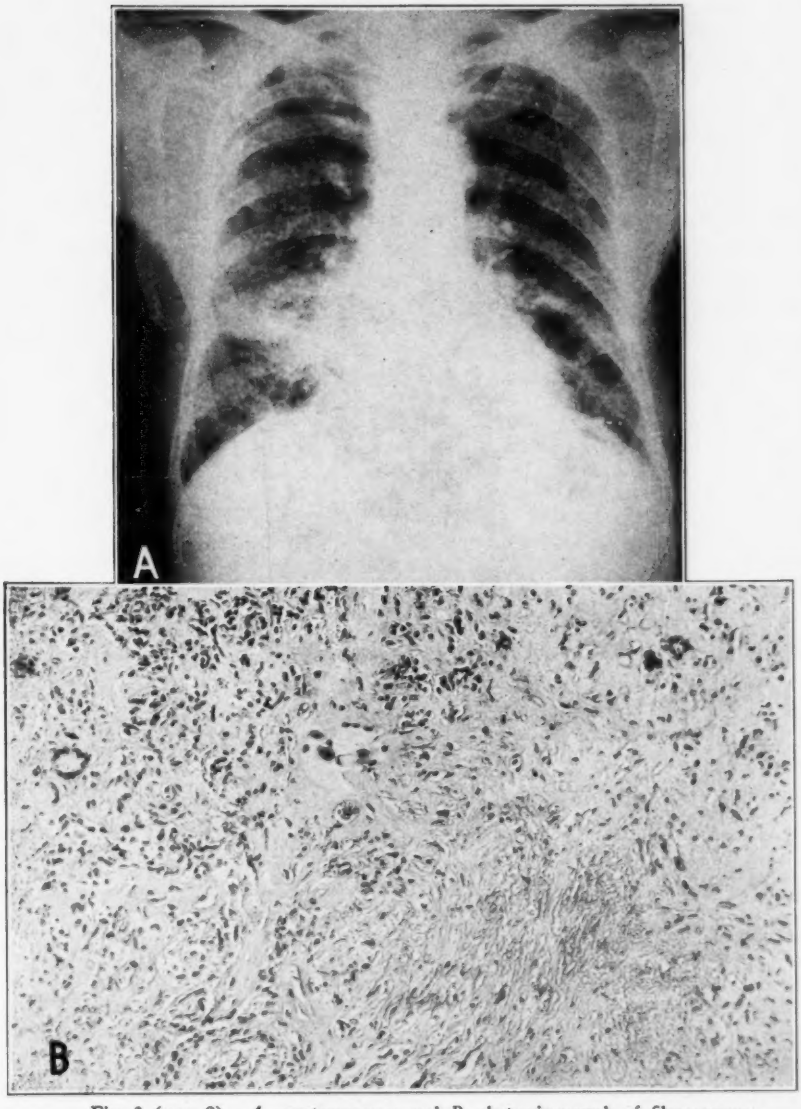

Fig. 3 (case 2).—*A*, roentgenogram, and *B*, photomicrograph of fibrocaseous tuberculosis.

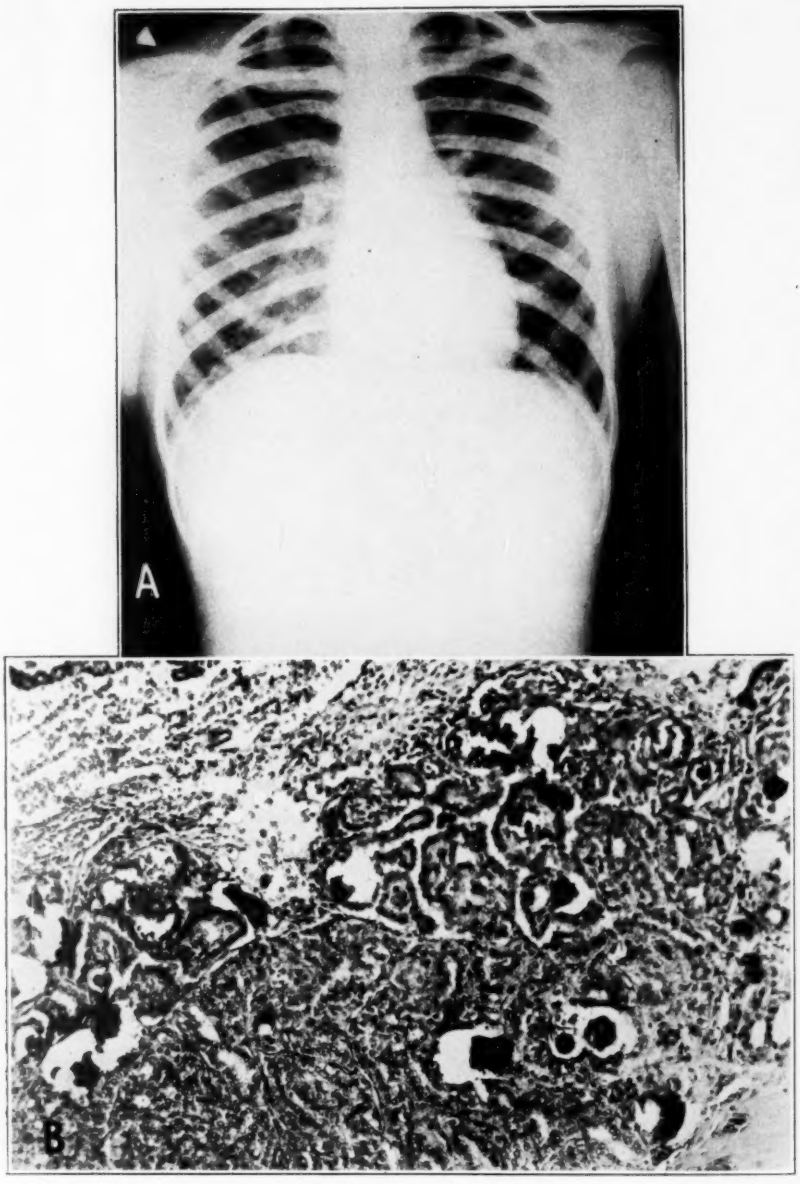

Fig. 4 (case 3).—*A*, roentgenogram, and *B*, photomicrograph of pulmonary metastasis from thyroid carcinoma.

surfaces, first on the superior surface (fig. 1, *6*) and, after transfixion at the site of the first mattress suture, back to the edge of the lobe on the inferior surface (fig. 1, *7* and *8*). The suture is now tied and cut. The suture produces hemostatic and air-tight closure (fig. 1, *9*).

A 14 F. catheter is placed into the pleural space, and the wound is closed by suturing the intercostal muscles with 00 silk, approximating the pectoral muscles and again suturing the skin. Because of the constant positive pressure anesthesia there is no necessity for the removal of air; however, 5 cc. of saline solution containing 100,000 units of penicillin is instilled into the pleural space and the catheter withdrawn. No postoperative drainage is used. The patient is allowed out of bed on the day of operation and is usually discharged on the third postoperative day.

REPORT OF CASES

CASE 1.—M. S., a 56 year old white railroad clerk, entered the hospital with the complaint of fatigue, dyspnea and pronounced loss of weight over a period of two years. A diagnosis of pulmonary carcinomatosis had been made elsewhere and radioactive isotope therapy recommended. Roentgenograms (fig. 2*A*) showed marked increased density in the hilar regions with irregular densities extending into the periphery of both lungs. Thorough examination of the patient failed to show the presence of a primary malignant tumor. Bronchoscopic examination showed nothing significant. Pulmonary biopsy revealed the lesion to be Boeck's sarcoid (fig. 2*B*). The patient returned to his regular occupation and has shown no progression of the lesion.

CASE 2.—R. B., a 38 year old Negro laborer, was admitted to the University Hospital for investigation of productive cough, pain in the chest and progressive dyspnea of nine years' duration. Roentgenograms (fig. 3*A*) of the chest revealed a diffuse hazy infiltration predominating in the lower pulmonary fields. Repeated examination and cultures of the sputum and bronchial aspirations were negative for acid-fast bacilli. The tuberculin and histoplasmin tests elicited negative reactions. Pulmonary biopsy revealed fibrocaseous tuberculosis (fig. 3*B*). The patient had an uneventful postoperative course.

CASE 3.—W. V. G., a 12 year old white boy, was admitted to University Hospital in severe respiratory distress due to tracheal compression by a thyroid tumor, first observed four weeks previously. Tracheal decompression was accomplished by partial resection of the tumor, which was found to be a thyroid carcinoma. Roentgen examination of the chest (fig. 4*A*) showed multiple miliary, fairly discrete densities in both lungs, apparently representing metastasis from the thyroid carcinoma. Radical resection of the primary tumor was not performed when pulmonary biopsy confirmed the roentgen diagnosis of pulmonary metastasis (fig. 4*B*). There has been regression of the lesion following radioiodine therapy.

CASE 4.—H. M., a 34 year old white nurse, entered the hospital with the complaint of a dry cough associated with a low grade fever of about four months' duration. Roentgen examination (fig. 5*A*) revealed a diffuse flocculent infiltration in the lower portions of both lungs. On repeated examinations sputum and gastric washing were negative for acid-fast bacilli. Boeck's sarcoid was suggested by the roentgenologist as a diagnostic possibility, and in the absence of enlarged peripheral lymph nodes a pulmonary biopsy was performed. When a metastatic

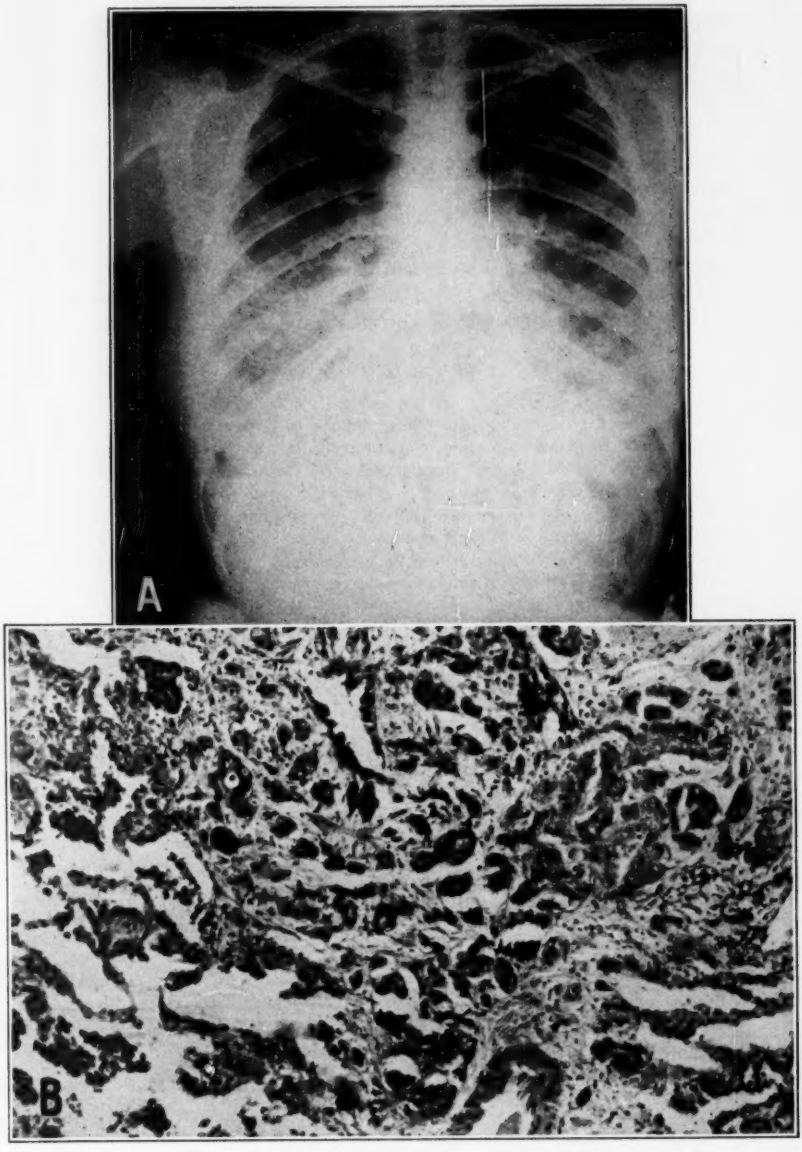

Fig. 5 (case 4).—*A*, roentgenogram, and *B*, photomicrograph of pulmonary metastasis from adenocarcinoma of breast.

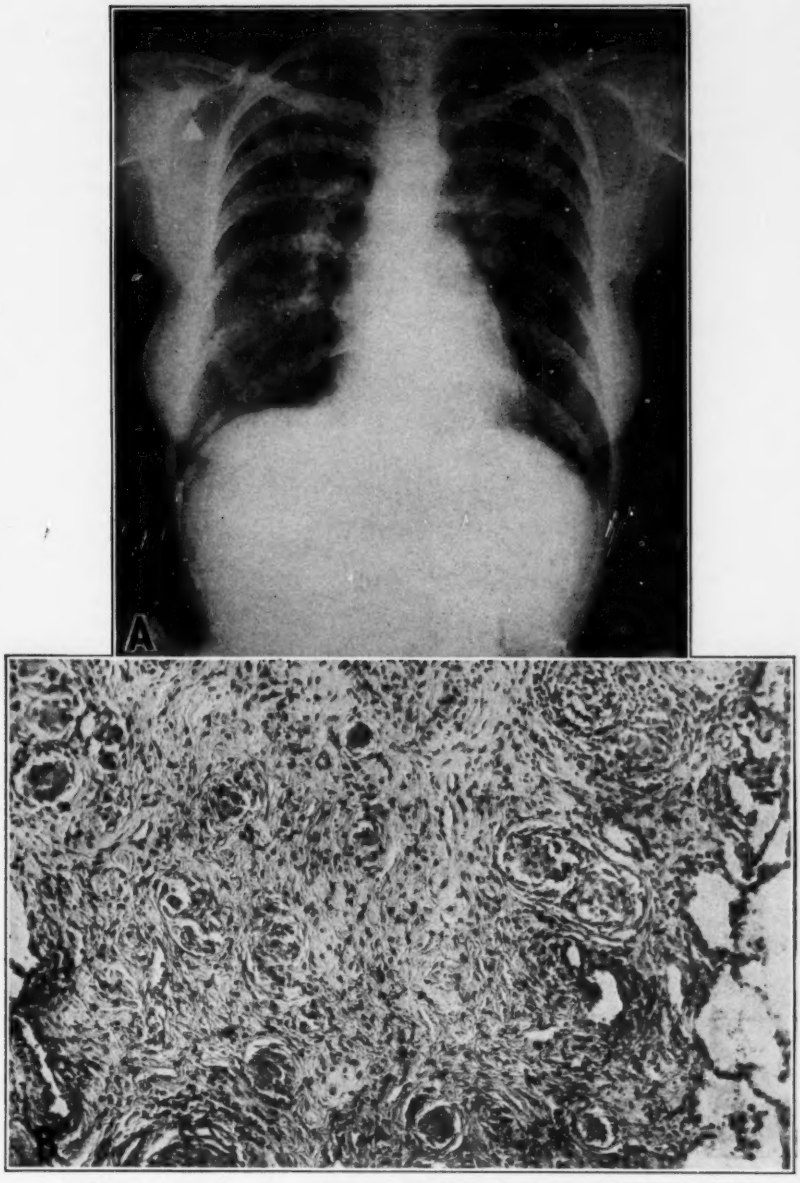

Fig. 6 (case 5).—*A*, roentgenogram, and *B*, photomicrograph of Boeck's sarcoid.

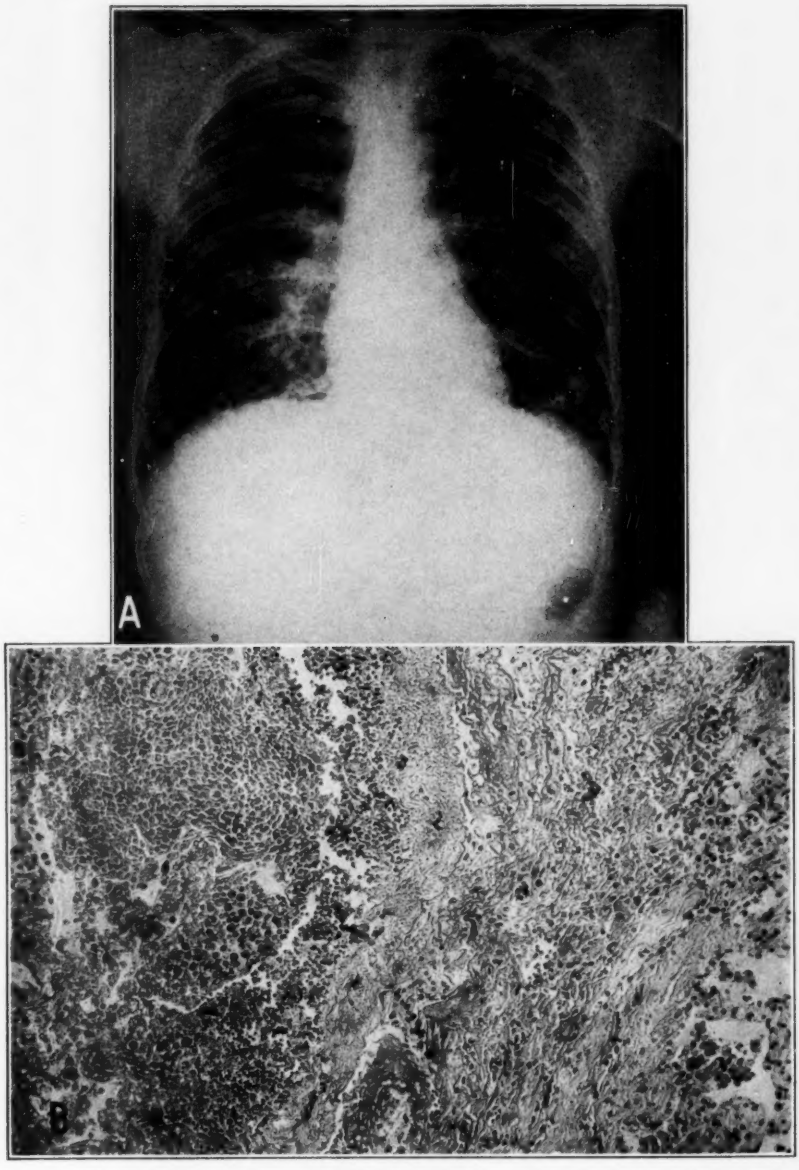

Fig. 7 (case 6).—*A*, roentgenogram of patient with metastatic malignant melanoma. *B*, photomicrograph showing good repair at site of biopsy.

adenocarcinoma was discovered in the pulmonary tissue (fig. 5*B*), a careful examination of the patient revealed the presence of a very small tumor in the right breast, later proved to be an adenocarcinoma.

Case 5.—E. G., a 41 year old white housewife, complained of a chronic cough which in the last year had become associated with fatigue, shortness of breath and a low grade fever. There was no improvement in her condition after a period of rest in bed. Roentgen examination (fig. 6*A*) showed diffuse miliary infiltration in both lungs. The patient's husband had been exposed to beryllium, and for this

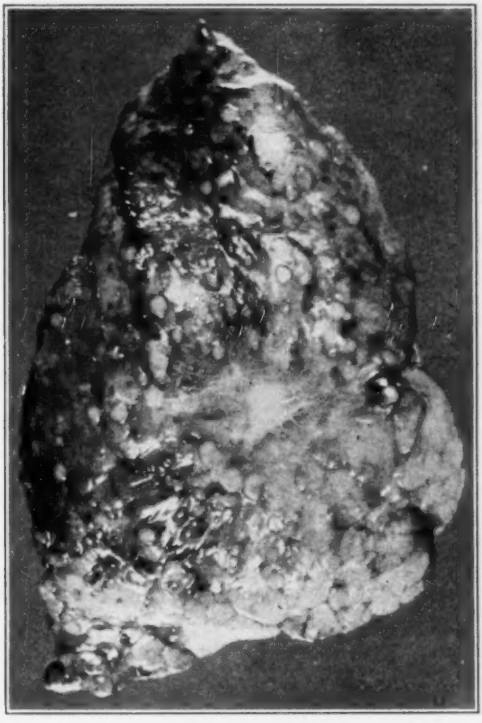

Fig. 8 (case 6).—Gross appearance at autopsy of lobe at site of biopsy.

reason a diagnosis of beryllium pneumonitis had tentatively been made. Sputum examination and blood studies were noncontributory. Pulmonary biopsy established a diagnosis of Boeck's sarcoid (fig. 6*B*). There has been pronounced clearing of the lesion without specific therapy.

Case 6.—A. H., a 45 year old white farmer, was admitted to the hospital with known widespread metastatic melanoma from a primary lesion on the right arm, treated previously by radical resection. Roentgenograms (fig. 7*A*) showed multiple diffuse fine nodular tumor metastases throughout both pulmonary

fields. A pulmonary biopsy was performed to observe the effect of an experimental drug on the malignant cells. The biopsy confirmed the preoperative diagnosis of melanoma metastatic to the lung. The patient tolerated the biopsy well but died of debility one week later. At autopsy it was observed that there was excellent healing of the pulmonary tissue at the site of the biopsy with minimal pleural reaction (fig. 8). Microscopic sections through the area of biopsy revealed excellent repair (fig. 7*B*).

COMMENT

Biopsy of diffuse pulmonary lesions has now been used in a series of 50 patients. The procedure was well tolerated by the patients and produced little discomfort. No complications occurred which could be ascribed to the procedure. There was no dissemination and no pleural or wound infection in patients with bacterial and fungous diseases. Neither pneumothorax nor hemothorax has occurred in our cases as proved by postoperative roentgen studies. Transient minimal subcutaneous emphysema developed in 2 patients with pneumoconiosis and compensatory pulmonary emphysema, which, however, did not require treatment. The biopsy site was examined at autopsy in 1 patient with extensive metastatic melanoma; it showed excellent repair (case 6).

Biopsy of diffuse pulmonary lesions has permitted a rapid, accurate diagnosis of such conditions as tuberculosis, histoplasmosis, pneumoconiosis and sarcoidosis, as well as primary and metastatic carcinoma of the lung when the conventional present day methods available failed to establish the true nature of the disease process.

SUMMARY

A method of biopsy of diffuse pulmonary lesions is described. An accurate diagnosis of the pulmonary lesion was made in a series of 50 patients by the pathologic, bacteriologic or chemical examination of the biopsy specimen. The surgical procedure as described was well tolerated by the patient, producing minimal morbidity and no mortality.

USE OF POLYETHYLENE IN EXTRAPLEURAL PNEUMONOLYSIS

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AND
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DENVER

THE OPERATION of extrapleural pneumonolysis for tuberculosis was apparently first performed by Tuffier in 1891.[1] In its various modifications this operation has enjoyed several periods of popularity, only to suffer ensuing periods of disrepute. In the armamentarium of conservative thoracic surgeons it has come to occupy a definite, though minor, place in their treatment of pulmonary tuberculosis. For the most part, its use should be confined to cases in which thoracoplasty cannot or should not be done. Literally scores of various and different substances have been used to fill the artificially created, unnatural extrapleural space. The recent introduction of comparatively nonirritating plastic compounds, particularly lucite (an acrylic resin, methyl methacrylate) in the form of spheres, has again brought this operation into focus.[2] However, the use of lucite spheres has been condemned by Trent,[3] Murphy[4] and others. The relative hardness of the spheres has caused them to erode into lung,[3] ribs[5] and esophagus, and because of their size and shape they have at times drifted into other anatomic localities.

In July 1947, Grindlay and his associates[6] first reported their experimental and clinical studies on polyethylene film. Their experience gave use the idea that this film might be a more suitable substance for filling the extrapleural space than those in current use. This supposition has since proved to be true.

Read at the Sixth Annual Meeting of the Central Surgical Association, Feb. 19, 1949.

1. Alexander, J.: The Collapse Therapy of Pulmonary Tuberculosis, Springfield, Ill., Charles C Thomas, Publisher, 1937.

2. Wilson, D. H.: Extrapleural Pneumonolysis with Lucite Plombage, J. Thoracic Surg. **17**:111-122 (Feb.) 1948.

3. Trent, J. C.; Moody, J. D., and Hiatt, J. S., Jr.: An Evaluation of Extrapleural Pneumonolysis with Lucite Plombage, J. Thoracic Surg., to be published.

4. Murphy, J. D., in discussion on Trent, Moody and Hiatt.[3]

5. Brown, R. K.: Personal communication to the authors.

6. Grindlay, J. H.; Brown, M. H., and Craig, W. McK.: Preliminary Report on Experimental and Clinical Studies with Polythene Film, Proc. Staff Meet., Mayo Clin. **22**:453-456 (July 17) 1947.

Polyethylene,[7] essentially a pure chemical compound,[8] a polymer of ethylene, is produced in the form of tough, flexible, elastic films of varying thicknesses. It is unwettable, light in weight (specific gravity 0.92) and transparent to roentgen rays and has a softening point above the temperature of boiling water.[6] Unlike many other plastic compounds, polyethylene holds sutures very well and has little tendency to tear. Grindlay found neither an inflammatory nor a foreign body reaction when polyethylene was buried in body cavities or tissues. Capillary-sized tubing inserted into veins has been left in place for as long as two weeks without plugging of the tube or reaction in the wall of the vein.[9] Thin films of polyethylene have been wrapped around severed tendons after suture and have very successfully prevented contiguous adhesions to surrounding structures.[10] We have implanted the film in the extrapleural space of dogs. Except for the initial effect of trauma produced by the operative procedure, no inflammatory reaction has been noted. The film lay as a completely inert material for as long as it was left in place. A great deal of confusion exists at present about tissue reaction produced by various types of polyethylene, and we do not wish to add more. Suffice it to say that the polyethylene film with which we have worked was apparently free from irritant plasticizers or other substances such as dicetyl phosphate which may have been used in the manufacture of this film for commercial purposes.[11]

Our clinical experience with polyethylene consists of its use in 21 cases of pulmonary tuberculosis for which extrapleural pneumonolysis was done. In the performance of this operation the posterior approach is used most frequently because we feel that better exposure is obtained than by the axillary or anterior route. A sufficiently long straight paravertebral incision is made to allow enough mobilization of the scapula so that a 3 or 4 inch (7.5 or 10 cm.) segment of either the third or the fourth rib may be removed. The cleavage plane separating the parietal pleura from the chest wall in the endothoracic fascia is

7. Supplied by the Visking Corporation, Terre Haute, Ind.

8. Cahn, E. B.: Personal communication to the authors.

9. Guenther, T. A.; Grindlay, J. H., and Lundy, J. S.: New Flexible Capillary Tubing for Use in Venoclysis, Proc. Staff Meet., Mayo Clin. **22**:206-207 (May) 1947.

10. Gonzales, R. I.: Experimental Tendon Repair Within the Flexor Tunnels: Use of Polyethylene Tubes for Improvement in Functional Results in the Dog, J. Bone & Joint Surg., to be published.

11. LeVeen, H. H., and Barberio, J. R.: Tissue Reaction to Plastics Used in Surgery with Special Reference to Telfon, Ann. Surg. **129**:74-83 (Jan.) 1949. Southworth, J. L.: Experimental Pulmonary Collapse, ibid. **129**:85-89 (Jan.) 1949. Yeager, G. H., and Cowley, R. A.: Studies on the Use of Polythene as a Fibrous Tissue Stimulant, ibid. **128**:509 (Sept.) 1948.

developed under direct vision. The size and contour of this artificially created space is determined by the localization and extent of the lesion. Usually the extent of the tuberculous process makes mandatory complete mobilization of the apex of the lung and separation of the parietal pleura from the mediastinal structures inferiorly to the aortic arch or the azygos vein. Once this space has been created, polyethylene film is inserted for its permanent maintenance. Initially a single large pack of fluffed-up film was roughly molded by hand into the general desired shape and inserted. We have found, however, that this type of pack shrinks somewhat in size in the following months (fig. 1). At present we are lining the cavity with a single thin sheet and then putting in long strips of the film to form a firm but resilient pack. This type of pack has not decreased in size as much as the former one (fig. 2).

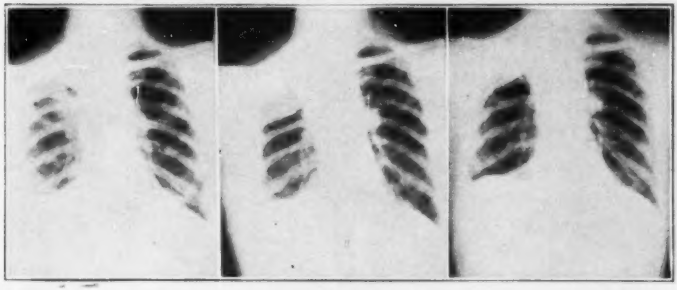

Fig. 1.—Decrease in size of an extrapleural polyethylene pack over a period of six months in a patient aged 62.

We have been rather conservative in our indications for the use of this procedure and have limited it largely to patients in whom thoracoplasty was not advisable—i. e., aged persons (our oldest patient was 65 years old), patients with preexisting contralateral thoracoplasty and persons whose pulmonary function precluded the less specific collapse afforded by thoracoplasty. There have been no deaths in this series of patients and no severe operative complications. Since our first use of this material, in December 1947, no patient has had a clinical infection of the extrapleural space. So far as can be determined, no erosion of an adjacent structure has taken place, and there has been no shifting in the location of the pack. The fact that closure of the cavity has not always taken place is due not to the substance used but to the inefficiency of the operation itself and the nature of the underlying disease.

Our clinical use of polyethylene film has shown it to have several distinct advantages. The film may be so used that it will completely fill the varying irregularities of the space. The pack may be made of any degree of hardness. It is easily sterilized, is easily handled in the operating room and requires no unusual instruments. Definitely advantageous is the fact that the material may be sutured to maintain its correct position. This characteristic was fortunately demonstrated when the free pleural space of 1 patient was inadvertently entered inferiorly at the completion of the stripping of the parietal pleura from the chest wall. The impossibility of closing this tear satisfactorily precluded the use of lucite spheres or paraffin. However, we were able to insert a polyethylene pack and suture it to the adjacent intercostal bundles. We have followed this patient's progress in the ten months since operation, and the pack has remained in its original position.

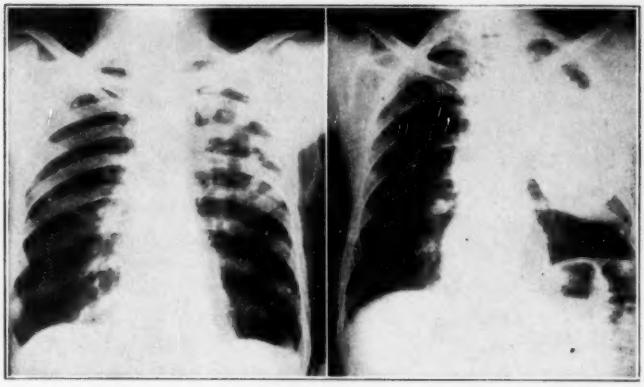

Fig. 2.—Large extrapleural polyethylene pack which did not decrease in size in a period of nine months (patient aged 65).

Such a pack may also be removed without difficulty. In 1 of our patients, closure of the cavity was not obtained, and nine months after the initial extrapleural pneumonolysis the pack was taken out easily and thoracoplasty performed because the patient's condition had improved sufficiently to permit that procedure. At the time of this operation the extrapleural space contained no free fluid and was not lined with a fibrous sac. In fact, after the pack had been in place for nine months, the cavity looked as though it had just been created and showed no gross visible reaction of any type. With positive pressure, the exposed lung covered by both visceral and parietal pleuras expanded fairly well. However, for academic reasons, a section of pleura was removed from the underlying lung; it proved to be a

layer of well organized fibrous tissue approximately 0.8 mm. thick. The pack itself was unchanged and had not deteriorated. When the various sheets of this pack were unfolded, they looked just as they had originally (fig. 3).

Our experience has shown that the disadvantages of this entire procedure have been those which are primarily inherent in the operation itself. Moreover, the fact that a polyethylene pack may decrease in size in the months after its insertion may or may not be a disadvantage.

Fig. 3.—Polyethylene pack removed from extrapleural space after nine months.

SUMMARY

Polyethylene film has been used as a filling in extrapleural pneumonolysis in 21 patients. It has fulfilled certain essential requirements and has so far been the best substance for this use that we have encountered. No attempt has been made in this presentation to evaluate the operation itself in its relation to pulmonary tuberculosis. However, we wish to emphasize our belief that it occupies a definite, though minor, place in our treatment of the disease.

"SPONTANEOUS" RUPTURE OF THE ESOPHAGUS

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MONTREAL, CANADA

In the byeways of surgery there can be few conditions more dramatic in their presentation and more terrible in their symptoms than spontaneous perforation of the oesophagus. No case has yet been treated successfully, and diagnosis has only been achieved in a very few before death, and yet there is no fundamental reason why this unsatisfactory position should not be improved in the future. Several things are essential to success: firstly, a knowledge that the accident can and does occur; secondly, a knowledge of the symptomatology; and, thirdly, an early diagnosis. Given these, I am convinced that surgeons will be able to save some of these patients by combining the principles, already well established in the cases of abdominal perforations, with those relevant to thoracotomy.—N. R. Barrett.[1]

WITH the preceding words, Barrett, in 1946, reported the fact that of 50 patients with spontaneous rupture of the esophagus whose cases were recorded in the world literature from 1724 to that date not one had survived. Several cases of survival have been reported in the past year; in the majority of them the condition was diagnosed only after rupture into the pleural cavity, and the subsequent course was a long and stormy convalescence.

It seemed, therefore, of value to report a case in which so-called spontaneous rupture of the esophagus occurred, the condition being detected and operated on before perforation of the pleura ensued, the end result being a rapid cure.

REPORT OF A CASE

A. D., a veteran, 30 years of age, while playing hockey sustained several very severe knocks, one in particular "knocking his wind out" completely. He paid no particular attention to this, however, and experienced no symptoms until the next morning. During breakfast he noticed a sudden, severe, burning pain in the pit of his stomach; in particular one piece of toast seemed to irritate something deep in his chest and he vomited. He went to work, but by 11 o'clock the burning pain was so severe that he could no longer stand. The burning finally became so severe that he requested admission to a hospital. On arrival, he stated that for about two years he had noticed the sensation when eating "as though food were

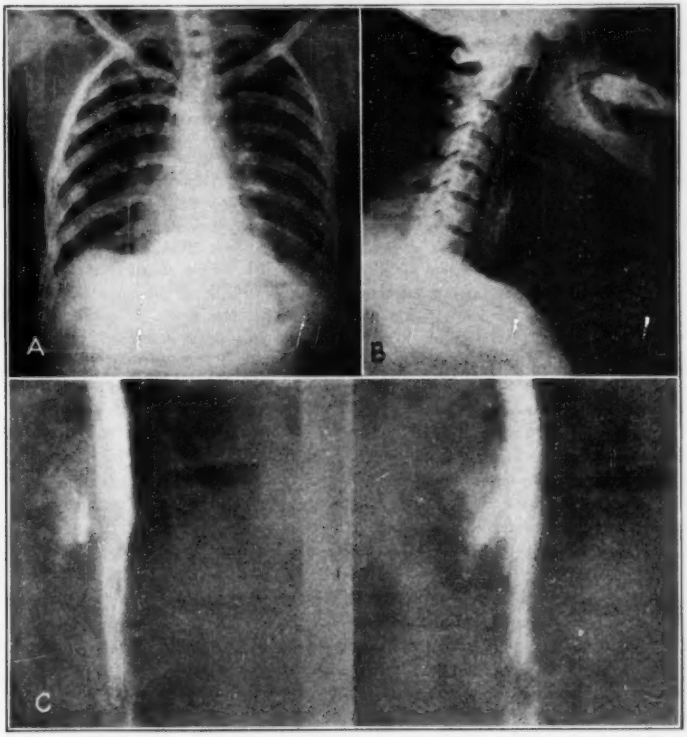
From the Queen Mary Veterans' Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 19, 1949.

1. Barrett, N. R.: Spontaneous Perforation of the Oesophagus: Review of the Literature and Report of Three New Cases, Brit. Surg. **1**:48 (March) 1946.

going down the wrong way." When this occurred he would leave the table and retch voluntarily. This seemed to clear this abnormal sensation, and he could then continue with his full and regular meal. There was no history of intolerance to any food or any other disease related to his gastrointestinal tract.

Examination on admission revealed a temperature of 99 F., a pulse rate of 88 and a respiration rate of 34. In addition to the rapid rate, the breathing was shallow and irregular. Examination of the chest revealed a few rales at the base of the left lung and short, shallow, rapid, irregular respiration of catching



A, apparently normal roentgenogram of the chest following perforation (this is one of the greatest causes of mistakes in diagnosis); *B*, lateral view of the neck showing column of air between the esophagus and vertebra; *C*, barium swallow showing escape of barium between the eighth and ninth vertebra.

type. Otherwise the chest and the cardiovascular system were normal. The blood pressure was 116 systolic and 56 diastolic. On examination of the neck crepitus could be felt.

The abdomen was tense and firm. The whole abdominal wall showed "guarding," more particularly in the upper quadrants. With persuasion this resistance

could be broken through. Tenderness was generalized, again more so in the upper half. No masses were palpable. No tenderness was detected in the lumbocostal region. (The abdominal condition was typical of that seen following perforation of a peptic ulcer.) Because of the rapid respiration rate, a roentgenogram of the chest was taken.

Within a few hours of admission the temperature reached 102 F.

In view of the rapid respiration, crepitus in the neck and rigidity of the abdomen a tentative diagnosis of rupture of the esophagus was made and a barium sulfate swallow was given. A curious conformation of the barium opposite the eighth thoracic vertebra confirmed the impression.

After establishment of the diagnosis a posterior mediastinotomy was done by the removal of the vertebral ends of the eighth and ninth ribs on the right side. The pleura was easily stripped away from the posterior thoracic wall and was intact, but as the esophagus was reached, the pleura was torn slightly and a small amount of clear, thin fluid drained from the right thoracic cavity. The esophagus was at first mistaken for the aorta because, instead of being soft and pliable, it was hard and indurated, actually resembling a length of rubber hose. The finger was slipped along the esophagus almost to the dome of the pleura, and only at this point did the esophagus begin to assume its normal consistency. As the finger was passed up, a considerable amount of thin purulent fluid came down from above. On closer examination at the level of the eighth thoracic vertebra, a small amount of pus was seen exuding from a tiny hole on the anterior surface of the esophagus. The outer coats of the organ at this point were opened and about a teaspoon of yellow pus, which seemed to have been contained within the muscular wall, was evacuated. A small hole into the mucosa was then found by a probe. It was impossible to determine the extent of this hole without doing serious damage to the esophageal wall. A Levin tube was then passed into the stomach from the mouth and two drains were installed: one, a Levin tube to the actual site of perforation, and the other, a sheath rubber drain to the hole in the pleural cavity. The latter was then packed off with gauze.

After operation the right lung was found to be collapsed and air was aspirated three times; thereafter full expansion occurred.

The packing and sheath rubber drain were removed in six days, the other drainage tube being left in place. One week following operation, the patient was allowed to drink and was also given methylene blue each day. The dye appeared on the thoracic dressing for five more days and then ceased. The Levin tube was removed from the stomach on the fifteenth day and the mediastinal drainage tube at the same time. All symptoms had disappeared in eighteen days, and on the twenty-first day the patient was on an unrestricted diet and was allowed to go home. On the twenty-sixth day he returned for examination and a small collection of pus was found in the wound, which was reopened slightly. However, dye given by mouth did not appear on the dressing, and a roentgenogram of his chest showed no abnormalities. All symptoms completely disappeared within forty-eight hours, and he has remained normal ever since. The usual antibiotic therapy was continued throughout his treatment.

Shortly before this patient was observed, the autopsy findings of a case of spontaneous perforation of the esophagus were shown in the hospital, and I had read Barrett's article, which emphasized the ease of diagnosis of this condition if the triad of symptoms is remembered.

The cause of this condition is unknown; hence the rather poor term "spontaneous." Apparently the precipitating factor is a sudden increase in intraesophageal pressure, brought on by forceful vomiting, straining or external trauma to the abdomen or thorax. In practically all cases coming to autopsy there is a tear in the esophagus, with mediastinitis and pleuritis. On microscopic examination of the tissues around this tear, lesions have not been found. One must conclude, therefore, that at the moment all theories as to the cause are purely speculative and the treatment is therefore empiric.

SUMMARY

A case of spontaneous rupture of the esophagus with cure is reported.

The triad of symptoms—rapid respirations, rigidity of the abdomen and crepitus in the neck—is emphasized.

The urgency of mediastinotomy is stressed.

No cause for the condition is known.

INTRAVENOUS ADMINISTRATION OF PROCAINE HYDROCHLORIDE DURING GENERAL ANESTHESIA

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BERT W. MARKS, M.D.
AND
GERALD EDMONDS, M.D.
DETROIT

THE RELATIVELY recent discovery of the fact that procaine can be administered intravenously to people without serious results and even with benefit in some circumstances, has stimulated renewed interest in the pharmacology of this drug. It has been taught for some years that inadvertent intravenous injection of procaine hydrochloride was very dangerous because of its tendency to produce serious systemic reactions in the form of either circulatory depression or generalized convulsions. While these teachings were not entirely erroneous, they must be revised to take into account the rate and concentration of injection.

Experiments carried out by Eggleston and Hatcher,[1] published in 1916 and 1919, furnished a background for the possibility of the intravenous administration of procaine. They reported that cocaine and holocaine® were destroyed rather slowly when administered intravenously but that procaine and several other drugs used for local anesthesia were rapidly destroyed when administered intravenously to animals. They were able to repeat a sublethal dose every twenty minutes in these animals without evidence of accumulation. Also, they were able to give the drug continuously, with the result that large amounts were well tolerated over a period of time. The drugs they studied produced similar symptoms when rapidly administered to animals in one sublethal dose. They reported that they usually found a fall in blood pressure, respiratory arrest, slowing of the pulse rate and a few generalized convulsions, and then the animal rapidly returned to normal. A known fatal dose caused prompt cessation of the heart and respira-

Read at the Sixth Annual Meeting of the Central Surgical Association, Feb. 19, 1949.

1. Hatcher, R. A., and Eggleston, C.: A Contribution to the Pharmacology of Novocaine, J. Pharmacol. & Exper. Therap. **8**:385-405 (May) 1916. Eggleston, C., and Hatcher, R. A.: A Further Contribution to the Pharmacology of the Local Anesthetics, ibid. **13**:433-487 (June) 1919.

tion usually combined with generalized extensor spasm. They believed that the drop in blood pressure was due to the action of the drug on the heart and not to vasodilatation. From in vitro experiments they concluded that the drug was destroyed by the liver. For measures of resuscitation they advised artificial respiration, with or without cardiac massage, and intravenous injection of epinephrine in cases of severe circulatory depression. These workers did not suggest any likely therapeutic value from intravenous use of procaine. They stated that the literature abounded with reports of severe toxic symptoms from the clinical administration of procaine and other drugs during the course of local anesthesia. Therefore, it is not to be wondered that the intravenous administration of these drugs was studiously avoided.

During the last ten years there has been an ever increasing use of procaine hydrochloride by the intravenous route. Lewy [2] reported administering procaine intravenously to treat tinnitus aurium; Lundy [3] used it by this route to treat pruritus, and Burstein [4] used it to depress cardiac irritability. The use of dilute concentrations, given over a period of time, for therapeutic purposes was reported by Graubard and Peterson.[5] Gordon [6] used procaine intravenously to relieve the pain for débridement of burns. McLachlin [7] used procaine by this route in relieving postoperative pain. Allen [8] was one of the first to use large amounts intravenously in an effort to produce analgesia for childbirth. He administered 1 to 2.5 Gm. per hour in a continuous intravenous drip and treated any convulsions that occurred with intravenous injec-

2. Lewy, R. B.: Treatment of Tinnitus Aurium by the Intravenous Use of Local Anesthetic Agents, Arch. Otolaryng. **25**:178-183 (Feb.) 1937.

3. Lundy, J. S.: Clinical Anesthesia, Philadelphia, W. B. Saunders Company, 1942, p. 392.

4. Burstein, C. L., and Marangoni, B. A.: Protecting Action of Procaine Against Ventricular Fibrillation Induced by Epinephrine During Cyclopropane Anesthesia, Proc. Soc. Exper. Biol. & Med. **43**:210-212 (Jan.) 1940. Burstein, C. L.; Marangoni, B. A.; DeGraff, A. C., and Rovenstine, E. A.: Laboratory Studies on the Prophylaxis and Treatment of Ventricular Fibrillation Induced by Epinephrine During Cyclopropane Anesthesia, Anesthesiology **1**:167-186 (Sept.) 1940. Burstein, C. L.: Treatment of Acute Arrhythmias During Anesthesia by Intravenous Procaine, ibid. **7**:113-121 (March) 1946.

5. Graubard, D. J.; Robertazzi, R. W., and Peterson, M. C.: Intravenous Procaine: A Preliminary Report, New York State J. Med. **47**:2187-2192 (Oct.) 1947; Microdeterminations of Blood Levels of Procaine Hydrochloride after Intravenous Injection, Anesthesiology **8**:236-240 (May) 1947.

6. Gordon, R. A.: Intravenous Novocaine for Analgesia in Burns, Canad. M. A. J. **49**:479-481 (Dec.) 1943.

7. McLachlin, J. A.: The Intravenous Use of Novocaine as a Substitute for Morphine in Postoperative Care, Canad. M. A. J. **52**:383-386 (April) 1945.

8. Allen, F. M.: Intravenous Obstetrical Anesthesia, Am. J. Surg. **70**:283-290 (Dec.) 1945.

tions of pentothal sodium.® Fraser [9] reported 400 intravenous administrations of procaine hydrochloride in 0.1 to 0.2 per cent solution in combination with pentothal sodium® during anesthesia. Barbour [10] reported on its use as a therapeutic drug, and Brodie, Leif and Poet [11] reported on the fate of intravenously administered procaine in man. Our interest in this therapy was stimulated by the report of Bittrich and Powers,[12] who used 1 per cent procaine hydrochloride solution intravenously during anesthesia and operation. They reported that it produced a depression of the cough reflex, decreased cardiac irritability and resulted in an inhibition of sweating. Although we have administered procaine in this way to approximately 400 patients, only a few more than 200 of the cases have been carefully analyzed. The only phase of this topic that will be discussed is the intravenous administration of procaine hydrochloride continuously during general anesthesia as an adjunct and not as the primary anesthetic drug.

Although this method can be used with almost any type of general anesthesia, our use of the drug has been limited to about three combinations. The first, and most frequently used method, consists in induction with pentothal sodium,® with or without curare, usually followed by endotracheal intubation and a continuous flow of nitrous oxide and oxygen plus intravenous administration of procaine hydrochloride throughout the anesthesia. This combination is frequently used in thoracic surgery, either for procedure on the thoracic cage or for transthoracic work. Another combination is the use of cyclopropane combined with administration of procaine intravenously. In still fewer instances, we have administered procaine intravenously in combination with ether anesthesia. It may be less important with ether, a drug which is efficient in depressing troublesome reflexes itself. However, one may maintain much lighter ether anesthesia and prevent excessive saturation of the tissues during a prolonged anesthesia.

The technic consists in making 500 or 1,000 cc. of 1 per cent procaine hydrochloride in 5 per cent dextrose solution by dissolving 1 Gm. of sterile procaine hydrochloride crystals to each 100 cc. of the infusion fluid to be used. This must be well shaken to insure complete dissolving of the crystals. This is administered through a needle separate from all other fluids, in order that its rate can be

9. Fraser, R. J.: Intravenous Pentothal Procaine Analgesia, Anesth. & Analg. **27**:159-163 (May) and 282-285 (Sept.) 1948.

10. Barbour, C. M., and Tovell, R. M.: Experience with Procaine Administered Intravenously, Anesthesiology **9**:514-523 (Sept.) 1948.

11. Brodie, B. B.; Leif, P. A., and Poet, R.: The Fate of Procaine in Man Following its Intravenous Administration and Methods for the Estimation of Procaine and Diethylaminoethanol, J. Pharmacol. & Exper. Therap. **94**:359-366 (Dec.) 1948.

12. Bittrich, N. M., and Powers, W. F.: Intravenous Procaine in Thoracic Surgery, Anesth. & Analg. **27**:181-196 (July) 1948.

carefully controlled. The rate is determined by counting the number of drops per minute, made possible by an ordinary dropper in the intravenous tubing. Administration of procaine is usually started shortly after surgical anesthesia has been produced by the principal drug, and the flow is started at a rate of 30 to 60 drops per minute, which amounts to about 2 to 4 cc. per minute or 20 to 40 mg. of procaine hydrochloride per minute. When pentothal sodium® is used for induction, there is no need for rapid rates of flow early in the anesthesia in most circumstances but it may be necessary to increase the rate as the effect of the pentothal sodium® decreases. The blood pressure must be watched carefully, and severe drops of pressure, regardless of the cause, indicate necessity to decrease or stop the flow of procaine until the cause of the drop in blood pressure has been determined and corrected. An average rate of 2 to 4 Gm. an hour is usually sufficient.

Clinical observation has revealed the following desirable effects from procaine during various types of anesthesia:

1. The cough reflex is depressed even when an endotracheal airway is in place or there is manipulation within the pleural cavity. This is not an absolute obtundation of the cough reflex, but it is a strong tendency to depress this reflex without otherwise deep anesthesia. Many times severe "bucking" has been controlled by procaine alone without interference with the patient's breathing.

2. It has been effective in preventing cardiac arrhythmias during most intrathoracic operations with cyclopropane. Again, this is not absolute but is a marked depressing effect on the cardiac irritability.

3. Sweating is inhibited; the skin remains warm and dry; occasionally the hands will be cool and dry. For the most part, this is a desirable action; however, it is possible that during hot weather depression of sweating will not be desirable.

4. The entire respiratory tract is usually very dry, and excessive salivation, nausea, retching and vomiting during recovery are very rare. The patients can retain fluids by mouth as soon as desired after recovery.

5. Intravenous administration of procaine is helpful in maintaining light anesthesia with any anesthetic drug, probably because of the drying of secretions, controlling of the cough reflex and producing of some analgesia. Many trials have demonstrated that it plays a part in maintaining anesthesia with light levels of surgical anesthesia.

6. It results in postoperative analgesia from twenty minutes to several hours, thus accounting in large measure for the recovery to consciousness without excitement. This has been particularly noticeable in patients recovering from cyclopropane.

7. The results in some types of operations are striking enough to be appreciated by both the anesthesiologist and the surgeon. The patients have been well pleased.

The disadvantages and dangers of intravenous administration of procaine hydrochloride are the following:

1. It increases the technical aspect of anesthesia by necessitating a separate infusion set and needle with careful control of the rate of flow. At the present time, we are able to get procaine crystals in 5 Gm. vials, and it is hoped that in the future procaine in solution may be available to avoid the necessity of dissolving crystals.

2. The greatest danger in the intravenous use of procaine is the possibility of circulatory depression, which may occur rather rapidly in case of an overdose. If pentothal sodium® is being used, this may occur without any convulsive manifestations being present. If cyclopropane is being used, this drop in blood pressure is rarely seen because convulsive manifestations usually occur before the circulatory depression. It is best to limit the rate of flow to 4 to 5 cc. per minute for an average adult and less for the elder patients.

3. The possibility of convulsive phenomena is always present; however, since we watch the patient constantly, we have no great fear of this complication because it can be controlled either by intravenous administration of a barbiturate or by decreasing the rate of flow of procaine. It is practically always preceded by facial twitching. Only once in 200 cases was pentothal sodium® given to control a convulsion.

4. There may be other dangers involved which we have not yet encountered, such as damage to parenchymatous organs or other tissue cells. Frequently, it takes several hundred cases to discover rarely occurring damage of this sort. To date, we have not observed any, in spite of fairly large doses to some patients.

There are three general types of operation in which procaine has been found the most advantageous. The first is thoracic or transthoracic operations; we have found it beneficial in depressing the periosteal and laryngeal reflexes, in depressing the cough reflex, in drying up secretions of the respiratory tract and also in providing postoperative analgesia. For intrathoracic operations it has been helpful in depressing cardiac irritability, but it has not been found that it is absolute in blocking vagovagal reflexes.

A second type of operation in which it has been found useful is in anesthesia for thyroidectomy. While the anesthesia for thyroidectomies does not present as serious problems as before the days of propylthiouracil, one can readily appreciate the stabilizing effect of intravenously administered procaine during this type of operation. The recovery has been smoother, and one is led to believe that a thyroid crisis might well be treated with intravenous procaine. The third group comprises operations of a superficial nature in which light anesthesia is adequate for the operative procedure. Such an operation can be performed either with

or without an endotracheal airway when procaine is administered. In these patients, smaller amounts of procaine are used.

Chart 1 is a copy of the anesthesia record during the intravenous use of procaine. It shows the patient's blood pressure and pulse during an intrathoracic operation. Induction was carried out with pentothal sodium,® cocaine was sprayed on the larynx, an oral endotracheal tube was inserted for the airway and the rest of the anesthesia was completed with nitrous oxide and procaine hydrochloride intravenously. The rate of flow of procaine is indicated in drops per minute. This patient received a total of 5 Gm. of procaine hydrochloride in one hour and

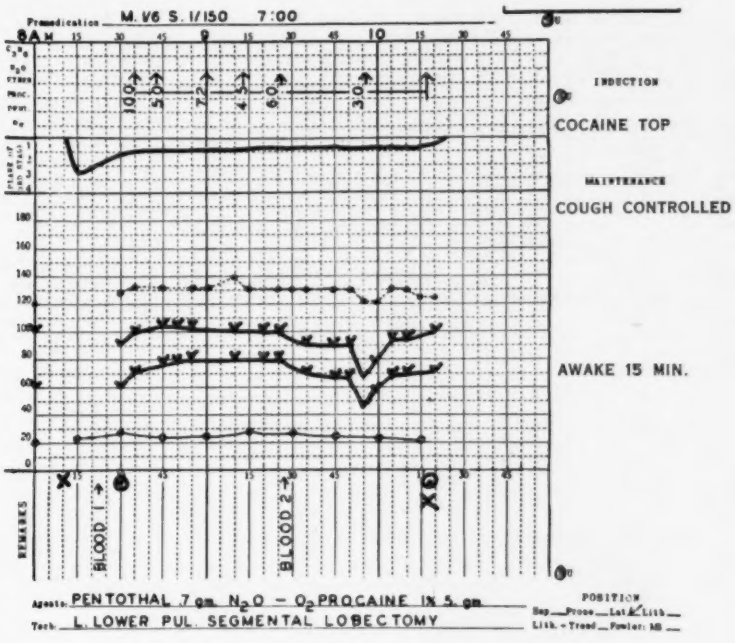

Chart 1.—Anesthesia record during an intrathoracic operation.

forty-five minutes. No pentothal sodium® was added after the induction, which was accomplished with 0.7 Gm. of the drug. Recovery to consciousness in this patient was slow, although reflexes were recovered immediately. The patient had twenty minutes' analgesia after return to consciousness.

Chart 2 is the record of anesthesia during thyroidectomy. The patient was a husky 30 year old man whose basal metabolic rate was no longer elevated after treatment with propylthiouracil. Induction of anesthesia was accomplished with pentothal sodium® mixed with d-tubocurarine and administered intravenously. The larynx was sprayed with 10 per cent cocaine solution before intubation. An oral endotracheal tube was inserted for an airway and used to replace the

mask. One point of interest in this case was a period of tachycardia that lasted some twenty minutes that was thought to be due perhaps to procaine, as the rate decreased after the rate of flow of procaine had been decreased. This patient received a total of 8 Gm. of procaine hydrochloride over a period of two hours and forty-five minutes. His recovery was immediate on discontinuation of the nitrous oxide and procaine; he had no vomiting and no pain and was not excited. It was not necessary to add any pentothal sodium® after the induction, even though there was an endotracheal tube in place and anesthesia with nitrous oxide was very light. The patient had no pain in his neck for thirty minutes after recovery to consciousness.

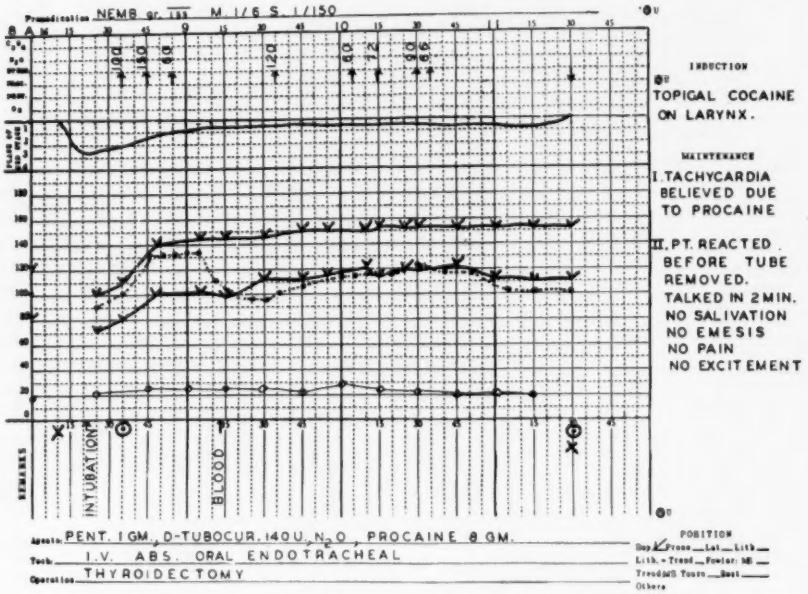
INDUCTION
TOPICAL COCAINE ON LARYNX.
MAINTENANCE
I. TACHYCARDIA BELIEVED DUE TO PROCAINE
II. PT. REACTED BEFORE TUBE REMOVED. TALKED IN 2 MIN. NO SALIVATION NO EMESIS NO PAIN NO EXCITEMENT
INTUBATION
BLOOD
POSITION
Agents PENT. 1 GM., D-TUBOCUR. 140 U., N2O, PROCAINE 8 GM.
Tech I.V. ABS. ORAL ENDOTRACHEAL
Operation THYROIDECTOMY

Chart 2.—Anesthesia record during a thyroidectomy.

Chart 3 is the record during anesthesia and operation on a 47 year old woman who had considerable hypertension before the anesthesia was started. The initial drop in blood pressure was produced by unconsciousness and the depressant effect of pentothal sodium® used for induction. The secondary depression of blood pressure was due to an overdose of procaine, as the blood pressure rose again after the rate of procaine was reduced. The second drop in blood pressure was intentionally produced by an overdose of procaine. The rate was increased to 120 drops, about 80 mg. per minute, and, after a period of ten minutes following a 20 mm. rise of systolic pressure, the blood pressure dropped. Softness of the pulse was noted, and the blood pressure was immediately taken; it was found that a drop of nearly 100 mm. of mercury had occurred. Use of procaine was immediately discontinued without changing anything else, and after a few minutes

the pressure again rose to its previous level. Except for weakness in pulse, reflecting the change in blood pressure, there were no other obvious changes in this patient during all this time. This a good demonstration of the rapidity with which circulatory depression can occur and the entire lack of warning signs except of the circulation itself. The drop in blood pressure is generally more gradual with ordinary rates of flow. One should not administer 1 per cent procaine hydrochloride faster than 6 cc. per minute and should then watch the circulation very closely.

Chart 4 presents the anesthesia record of a 74 year old man who was mentally confused before operation. He had auricular fibrillation, avitaminosis,

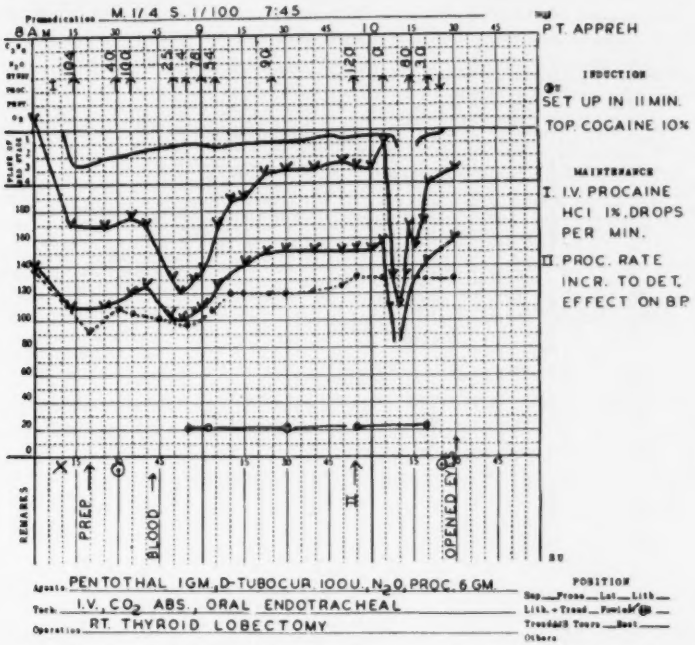

Chart 3.—Anesthesia record during an operation on a patient with hypertension.

generalized arteriosclerosis, chronic alcoholism and a fracture of the neck of the left femur. Anesthesia was induced with pentothal sodium® intravenously, followed by nitrous oxide and oxygen and procaine by the intravenous route. An overdose of procaine resulted in a marked drop in blood pressure and a complete disappearance of pulse. Respiratory arrest also occurred; the patient was definitely cyanotic. Vigorous inflation of the lungs with oxygen did not improve the patient's color. This obviously meant that the cardiac action was either stopped or insufficient. Epinephrine hydrochloride (1 mg.) was injected intravenously and forced in by intravenous solution. Thirty seconds later a palpable pulse was noted, and in two minutes the patient's color improved and in about five minutes the blood pres-

sure had returned to a fair level. After fifteen minutes, the respirations were resumed by the patient, although there was no light reflex of the pupils. The operation was not done. On the following day, the patient returned to his previous mental state; one week later, the operation was performed under open drop ether anesthesia. This represents the nearest to a fatality that has occurred in our series. The trouble was due to failure to observe the patient's circulation closely and also to the excessive dose of procaine to an elderly patient. It has been found that only about half the amount of procaine is necessary for elderly as for younger patients.

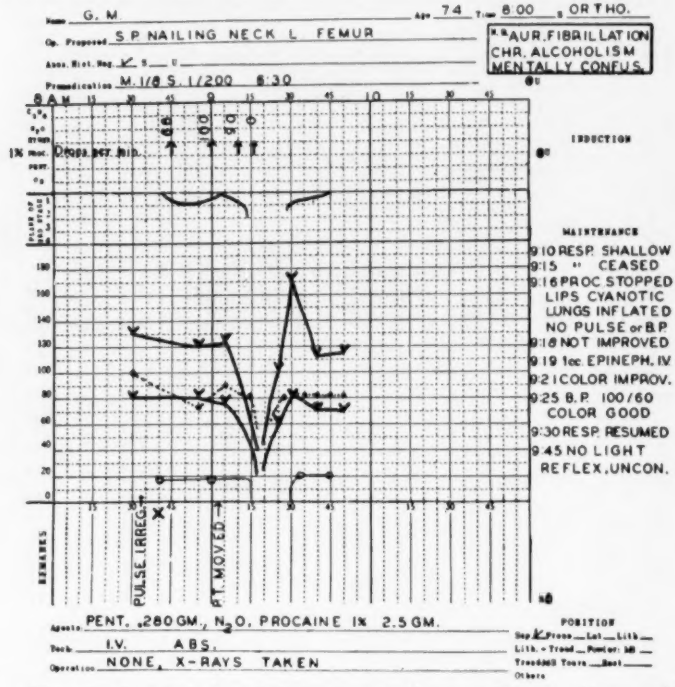

Chart 4.—Anesthesia record during an operation on a 74 year old man with avitaminosis, auricular fibrillation and generalized arteriosclerosis.

COMMENT

The use of 1 per cent procaine hydrochloride intravenously during general anesthesia has a definite value in certain type of anesthesia. The chief danger is circulatory depression caused by an overdose. This potential hazard may prove to be of sufficient magnitude to preclude the use of this drug in sufficient quantity to be of value. At the present time it appears that use of a sufficient quantity to assist in producing anesthesia places the method in the same category as the administration

of deep cyclopropane or chloroform anesthesia as far as the alertness necessary in watching the circulation is concerned. Lower and safer doses are of benefit in depressing some reflexes and are preferred in the light of the experience to date. Hence, 4 cc. per minute is the maximum for young adult patients, and not more than half that amount should be given to elderly patients The effect it may have in preventing edema under casts or in the operative field has not been studied but has been suggested by Gordon.[13] For the most part, the use of procaine in this way represents a new purpose for a drug during anesthesia, and probably we are not too well prepared to measure its benefits. It has been appreciated for some time, however, that most drugs that produce general anesthesia are lacking in power to depress certain reflexes and functions, even though in most respects they are highly desirable. Ether is one drug that in higher concentrations depresses nearly all reflexes, and its over-all safety is recognized, but it is not pleasant for most patients and disturbs metabolism considerably. It is possible that better anesthesia will be possible with drugs like nitrous oxide and pentothal sodium • if procaine can be safely administered by the intravencus route.

13. Gordon, R. A.: Application of Intravenous Procaine Therapy in the Surgery of Trauma, read at Congress of Anesthetists, Montreal, October 21, 1948.

SURGICAL TREATMENT OF LOW BACK PAIN WITH SCIATIC RADIATION

Preliminary Report on Three Hundred and Forty-Six Cases

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AND
GEORGE R. GRANGER, M.D.
DETROIT

ALTHOUGH there are already many articles on the subject of low back pain with sciatic radiation, we feel that our experiences may be worth recounting because (1) from the beginning such treatment has been a joint project of the orthopedic and neurosurgical divisions of this hospital and (2) because from it we have developed certain concepts that seem a little different from those commonly expressed in most of the other reports.

We wish to place emphasis upon three main points which we intend to make in this report. The first is that disturbances of the intervertebral disks may be but a part of a more general dysfunction involving the vertebral and related structures. We feel that these lesions which do not show frank pathologic changes in the disks should receive greater emphasis than they have in the past. The second is that we recommend uncapping of the nerves (especially the fifth lumbar) in all cases in which the disk is not the obvious compressing factor. The third is our experiences regarding fusion which have led us to maintain an intermediary position regarding its use.

Our report comprises 346 consecutive cases in which the diagnosis of "nerve compression syndrome" had been made by both divisions during the last seven years. We, by common consent, used the more general term, "nerve compression syndrome," [1] because in our early experience only about 40 per cent of the cases showed frank extruded or protruded segments of disks and the rest showed various other

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From the Orthopaedic and Neurosurgical Divisions, Henry Ford Hospital, Detroit.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 19, 1949.

1. Crawford, A. S.: Nerve Compression Syndrome of Lumbar Nerves: Modern Concepts and Surgical Treatment, J. Maine M. A. **36**:183-188 (Nov.) 1945.

abnormalities which at first we did not correlate, but which now seem to us to fit into a definite entity. We are omitting the data on sex, age, relationship of trauma and results of spinal fluid and neurologic examinations, as they do not contribute anything not already brought out in many excellent reports published previously.

In choosing patients for operation we have tried to maintain a conservative attitude. Patients with acute conditions were treated conservatively for from two weeks to several months if there was improvement. Chronic or recurring conditions were considered surgical when the severity and duration of pain and disability seemed to warrant the more radical form of treatment.

In the majority of cases some or all of the signs and symptoms of nerve compression syndrome were present: (1) diminution of the ankle or knee jerk; (2) positive Lasègue sign with or without pain on straight leg raising; (3) hypesthesia over one or two dermatomes; (4) weakness of one or several muscle groups; (5) list of the spine; (6) muscle spasm of the lumbar region and pain on movement of the trunk; (7) tenderness on palpation over the affected lumbar facet and/or over the sciatic nerve, and (8) pain of the typical nerve root type in the distribution of the fourth or fifth lumbar and/or first sacral dermatomes.

In establishing the diagnosis we considered most carefully the history and the neurologic and roentgen findings; in 206 cases we also used myelography as corroborative of other diagnostic criteria. This was also useful in showing multiple and bilateral lesions and helped us to plan the surgical attack more intelligently.

Earlier in our experience we concentrated on the intervertebral disk and assumed that the removal of the ruptured segment was sufficient to relieve all the pain; but there were so many of our patients who reported either a return of the old pain, occurrence on the opposite side or a troublesome stiffness or ache in the back on exertion that we began trying a number of more radical procedures in the hope of curing a larger percentage of patients and of learning the reason for the failures. There were 385 operations on 346 patients (table 1). There were no deaths in the series.

It should be stated that from the beginning we have advocated adequate exposure. We found that a square-shaped interlaminal opening made with an osteotome and chisel gave better access to the disk and overlying nerve than the round window made with a rongeur. The protruding portion of the annulus was excised, and the soft, degenerated nucleus pulposus was curetted out, not too vigorously. For better removal of an extruded segment of disk, the opening was often enlarged laterally and upward. It was this part of the technic which

led us gradually to the conviction that the compression of the nerve was often due to a combination of forces—the protruded or prominent disk compressing anteriorly, and bony, ligamentous and fibrous tissue compressing from behind and laterally.

Hence our present conception of this problem is that the protruding disks are but a part of the structural dysfunction which involves any or all of the several structures that make up the various joints of the vertebral column. In some cases it is protrusion of the disk that is most evident; in others the prolapse results in bulging or swelling of the ligamentum flavum [2] and/or hypertrophy of fibrous tissue of the joint capsule. The downward prolapse also brings closer together the narrow walls of the intervertebral foramen.

These abnormalities are not evident unless one removes the inferior articular process and that portion of the superior articular process which overlies the nerve in the foramen. This is referred to subsequently as uncapping of the nerve. The nerve most commonly affected is the

TABLE 1.—*Operative Procedures**

Procedure	No.
Unilateral hemilaminotomy	168
Bilateral hemilaminotomy	86
Hemilaminotomy and uncapping of nerve	83
Bilateral hemilaminotomy and uncapping of nerve	26
Bilateral laminectomy, sparing facets	10
Removal of neural arch	12
Total	385

* Including 39 secondary operations.

fifth nerve, which passes through the most constricted of the foramens.[2] Another observation, which has been noted particularly in cases of abnormal mobility, such as spondylolisthesis and spina bifida, is that the base of the lamina which lies next to the fifth nerve at its entrance into the foramen can cause direct impingement posteriorly on the nerve, with increased extension at that joint.

Our operative experiences have shown us that it may not be enough to remove a ruptured disk segment, even though the case is clearcut; so we now routinely follow this procedure by a thorough probing outward in the foramen, feeling for any constriction or tissue which might compress the nerve. If we are not certain that there is plenty of extra space, we proceed to uncap the nerve, removing all the compressing structures. After this procedure is complete, we then cover the exposed nerve with a thin piece of fatty tissue with the hope that it will lessen the amount of fibrous tissue that will form

2. Larmon, W. A.: An Anatomic Study of the Lumbo-Sacral Region in Relation to Low Back Pain and Sciatica, Ann. Surg. **119**:892-896 (June) 1944.

later. Spurling and Grantham have mentioned in their recent report [3] that in some cases with negative findings relief was obtained by uncapping of the nerve.

In 122 of our operations nerves were uncapped as a part of the procedure. From an analysis of these cases it seems that some benefit was derived from this part of the operation. It is not possible to prove this statistically because of the several procedures combined in some of the cases, but we do feel that our results, in general, are improving, and we are inclined to give at least some credit to this procedure. As to the charge that uncapping of the nerve increases instability of the back, we know of only 2 cases in which subsequent fusion was necessary because of backache. Table 2 shows the operative findings in our cases.

The last item in table 2 includes the various structures referred to previously. Undoubtedly, some of the 73 lesser abnormalities of disks were also partly due to the other compressing structures but were not

TABLE 2.—*Operative Findings*

	Cases	
	No.	%
Ruptured and/or extruded disks	142	40
Protruding or prominent disks	73	20
Negative findings	8	2
Sclerosing osteitis (laminal thickening)	9	38
Tumor (schwannoma) of the fifth lumbar nerve	1	
Other compressing structures (bony, ligamentous, fibrous, etc.)	113	
Total	346	

discovered at the time because in some cases the nerves were not uncapped. So it can be seen that in our series, 40 per cent were frank instances of a ruptured disk; another 20 per cent were called "prominent disks," but the condition may have been due to additional pathologic changes unrecognized at the time, and in 38 per cent it was due to compression of a nerve in or around the foramen.

It should probably be pointed out that we explored almost routinely both the fifth and the fourth lumbar disk because of the relative frequency of pathologic disks at these two sites. This was done bilaterally if in the history it was revealed that there had been trouble on both sides. Table 3 shows the relative frequency anatomically of the disks found at the operation.

As to the third point, fusion, the subject of combined operation for the nerve compression syndrome has been a controversial one for a number of years. Many papers have been written on this problem with a variety of criteria and recommendations for fusion, ranging from those

3. Spurling, R. G., and Grantham, E. G.: The End-Results of Surgery for Ruptured Lumbar Intervertebral Discs, J. Neurosurg. **6**:57-64 (Jan.) 1949.

urging fusion in all cases to others expressing the belief that fusion is never necessary. Other observers, after thorough consideration of the problem, have concluded that there are no criteria for spinal fusion following removal of a protruded nucleus pulposus.

Inasmuch as we had so many patients with early or late return of pains in the leg and back after routine removal of a disk, we performed more and more primary fusions on a trial basis. Table 4 shows the types and number of each.

TABLE 3.—*Anatomic Location of Pathologic Disks*

Vertebra	No. of Cases	
Second lumbar	1	
Third lumbar	3	
Fourth lumbar	66	98%
Fifth lumbar	106	
Fourth and fifth lumbar	38	
Third, fourth and fifth lumbar	1	

TABLE 4.—*Fusion Operations**

Type	No.
Albee	10
Modified Hibbs	57
Plug (iliac crest, Cloward)	11
Facet	8
H type	11
Simple prop or strut	29
Total	126

* Including 23 secondary operations.

TABLE 5.—*Results*

	Cases	
	No.	%
Good to excellent	211	61
Fair to good	40	12
Poor *	95	27
Total	346	

* Including 10 failures.

Each of these methods seemed to have satisfactory results in a majority of cases. The objections to most of the methods of fusion that we have used in the past were that (1) too high a percentage of nonunion resulted, (2) the period of immobilization following operation was necessarily prolonged and (3) it was difficult to establish fusion which would separate permanently the interspaces posteriorly.

Since we have utilized the prop type of graft, the results appear to have been more uniformly successful, although it is too early yet to

draw definite conclusions. The type of graft used in this method of fusion is locked securely in position and tends to keep the fourth and fifth interspaces from collapsing. The patients have been allowed up in a plaster lumbar support fourteen days after operation.

The preliminary results since the method was adopted, almost one and a half years ago, have been extremely gratifying. But it is realized that a longer follow-up period will be necessary before final conclusions can be drawn.

As to the end results in our series, we are in the process of working out a method of evaluating results which uses subjective as well as objective data. We plan to report this in a subsequent communication, but we can give the results that are recorded to date. All the patients have been followed for at least three months; some have had a follow-up period of nearly four years.

We can state that 211 patients, 61 per cent, were at work and with no complaints in from three months to over three years. This group we graded from 85 to 100 per cent, and the results were classed as good to excellent. There were 40 patients, 12 per cent, who returned to work but still had occasional trouble with the back or legs. This group we graded from 60 to 84 per cent and called the results fair to good. There were 95 patients, 27 per cent, who had more complaints than the second group. These results we considered poor. There were 10, 2 per cent, for whom results should be considered failures, although most of them are still doing some work.

In the group with poor results there were 39 reoperations on 35 patients. Of these reoperations, there were 23 fusions on 22 patients and 17 reexplorations without fusions. Of the 22 patients with secondary fusions there were 12 who had good results, 4 who had fair results and 4 who had results graded as poor; in 1 the result was a failure, and 1 did not return for examination. Of the 17 patients with nonfusion operations, 9 had good results, 2 fair, 4 poor and 1 failure; 1 was not heard from.

SUMMARY

We are reporting a series of 346 consecutive cases of nerve compression syndrome in which there were 385 operations.

In 40 per cent of cases frank ruptured disks were found; about 20 per cent showed less definite pathologic changes in the disk, and there were 38 per cent in which the pathologic process involved the other vertebral structures. In about 2 per cent the findings were recorded as negative.

We advocate an adequate exposure of both the fourth and the fifth lumbar disk on one or both sides according to the history, myelograms and operative findings and good surgical removal of the accessible degenerated segment of disk.

We also advocate uncapping of the nerves, at least the fifth lumbar nerve, unless one can be certain after thorough probing that the nerve is not in danger of compression in the nerve canal. In some cases of well marked disease of a disk there is also nerve compression in the foramen, which explains persistence of pain after removal of the disk.

We advocate primary fusion in cases in which there has been a long history of pain in the back or legs and in which there is roentgen or operative evidence of instability to make this procedure justifiable. We have found by experience that a strut or prop type of graft has given us the most satisfactory results. By good coordinated team work the operative time for this combined procedure can be cut down considerably, and with this type of graft, ambulation and convalescence can be shortened.

CONCLUSIONS

This report is intended as a statement of our combined experience and present impressions. During the last year our results have been more satisfactory as a whole than any we previously obtained. At present we feel convinced that these better results are being gained by the more careful searching for the nerve-compressing structures (disk and nondisk), uncapping of the nerves wherever indicated and primary fusion in all cases in which this seems indicated. In a subsequent report we will be in a better position to evaluate the end results. We can then see whether we are able to maintain our present concepts.

DISCUSSION OF PRECEDING PAPERS

DR. HERMAN E. PEARSE, Rochester, N. Y.: If you look into the antiquity of the literature, you will notice that at one time I studied the fascial planes of the neck and the mediastinum in relation to the spread of infection. Because of those observations, I should like to point out that one observation in the case reported by Dr. Gardner is unusual.

The lateral view showed air behind the pharynx in a fascial space ordinarily termed the retropharyngeal or retrovisceral space. This extends from the base of the skull to the sixth dorsal vertebra. In perforations of the upper part of the esophagus it is the path of spread of infection, and, of course, these are very common in traumatic lesions from foreign bodies or esophagoscopy. This space must be drained. It can be approached easily through the neck. On the other hand, perforations below the sixth dorsal vertebra may cause emphysema in the neck, but they ordinarily do not fill the retropharyngeal space with air. Hence I merely wish to mention that in the majority of subjects the sign presented by this patient will not be found, and one will not have roentgen evidence of involvement of the retropharyngeal space from a perforation of the esophagus at the level of the eighth dorsal vertebra.

DR. A. J. ANLYAN, Columbus, Ohio: In reviewing the etiology of spontaneous rupture of the esophagus, I think I should mention a case that was brought to my attention in Columbus.

A 56 year old woman had an abdominal operation and was duly sent down to her room under the charge of her private nurse, with a Levin tube in her stomach. The nurse proceeded to hook up her Levin tube to the oxygen tank. We were called in, and the patient had a tremendous subcutaneous emphysema. She was too sick to undergo any surgical or endoscopic measures at that time, and we just instituted complete antibiotic therapy and watched her; ten days from the date of her perforation she was home, feeling well.

Dr. John H. Grindlay, Rochester, Minn.: I do not believe that I can add much to what Dr. Condon has told you about polythene. I might say again, however, that the fibrous tissue reaction which he described about the pack is truly a very minimal reaction. He said that the thickened pleura under the pack was only about 0.5 mm. thick. I have found that the fibrous tissue layer about polythene is thickest in the first few weeks after the film has been implanted. After film has been in place longer than six weeks, the fibrous layer is very thin and when one examines it histologically there are very few cells to be seen. The layer consists of collagenous fibers all oriented in the same plane and direction, and in cases in which we have used it to fill dural defects it resembles dura very closely.

I think that the procedure Drs. Condon and Harper have proposed is a very definite contribution. I hope and believe that it will stand the test of time. Dr. O. T. Clagett and I have been working on dogs in a somewhat similar study. We have placed a sealed bag of polythene film, filled with spun glass, into the pleural cavity after pneumonectomy in order to prevent overdistention of the remaining lung. Our early results were very encouraging, but, unfortunately, the material is not tough enough to stand up more than a few months. After four to eight months a crack develops or a seam bursts, and until a means of getting a better constructed bag is found I am afraid our study is at a standstill. One of the things which has encouraged us, however, is the observation that polythene produced virtually no thickening of the pleura.

Dr. Cameron Haight, Ann Arbor, Mich.: Drs. Klassen, Anlyan and Curtis have emphasized the need for biopsy of certain pulmonary lesions in which a diagnosis otherwise cannot be made. One of the factors which has hitherto retarded progress in this direction has been the fear of complications following incision of the pulmonary parenchyma in conditions of a possibly infectious nature. It is noteworthy that Dr. Klassen and his associates have not experienced any complications in their series of 50 consecutive cases. They are to be congratulated on their use of a definitive procedure to obtain a diagnosis of otherwise obscure lesions.

The use of polythene film, as recommended by Drs. Condon and Harper for the maintenance of extrapleural collapse of the lung, is presented by them because of its nonirritating qualities. In this respect it should prove to be highly desirable. Certain objections are inherent, however, in the operation of extrapleural pneumonolysis because of the space which is thereby created. The collective experience of many surgeons with the introduction of foreign material in order to maintain selective pulmonary collapse has shown that any type of foreign body, including air as used in extrapleural pneumothorax, may sooner or later lead to complications. Certain materials, such as paraffin, with which we have had considerable experience at the University of Michigan, and even more so the lucite balls, with which we have had no experience, possess the disadvantage of providing an irregular, firm contour which may cause localized areas of pulmonary necrosis. The softness of polythene film should be of definite advantage in lessening the objection to the other materials. There is always the possibility in any case of

extrapleural pneumonolysis that infection of the extrapleural space may occur. In particular, tuberculous infection is the type of infection most commonly encountered in these cases. It occurred in a small percentage of our cases with paraffin filling and was usually a delayed complication, being first evident between six months and four years after operation. Principally because of this complication, collective experiences with the various types of extrapleural pneumonolysis used to date have shown that the initial enthusiasm soon dampens. This was also the case with the soft type of filling, the flexi-tissue,* used by R. C. Matson and described by him in 1942. Although polythene film possesses the particular advantage of inertness, we should not endeavor to evaluate the results until an adequate period of observation has been possible.

Dr. William Tuttle, Detroit: My colleagues and I have used procaine hydrochloride axan anesthetic agent for about the last year and a half. We have used it in a large number of thoracic operations. We think that that it has certain very definite advantages. The patients wake up quickly after the operative procedure, even though the procedure is sometimes prolonged. This is a distinct advantage because it makes possible the patients' coughing early and eliminating secretions more advantageously. We feel that they definitely have less postoperative pain. We have seen no reason not to use this type of anesthetic. In fact, we have become fond of it and feel that it is certainly much better than any type of anesthetics we have had previously for thoracic procedures.

Dr. K. P. Klassen, Columbus, Ohio: In answer to Dr. Haight's comment I wish to state that owing to the air-tight and hemostatic stitch used in our method of pulmonary biopsy, obliteration of the pleural space occurs immediately and thus infection will not occur. I have seen no cases of tuberculous sinus following this procedure in patients with pulmonary tuberculosis.

Dr. C. McG. Gardner, Montreal, Canada: Dr. Pearse's comment brings up a rather important point. I have had the opportunity of operating on 2 patients whose esophagi had been perforated by instrumentation, and in neither of them did interstitial emphysema occur. Nevertheless, in the group of cases reported by Ridgeway, including many of the papers on spontaneous perforation, some 40 cases in all, interstitial emphysema occurred in the vast majority, although the rupture usually occurred opposite the eighth or ninth dorsal vertebra. This puzzled my colleages and me.

We obtained a number of esophagi from cadavers and applied intraluminal pressure, sometimes below, sometimes above. The esophagus nearly always split opposite the eighth vertebra. I believe that pus then tracks up within the esophageal wall and bursts out opposite the fifth or sixth vertebra. Whether this explains the fact that the interstitial emphysema occurs so often in these cases with spontaneous rupture, I do not know, but it is an interesting thought.

Dr. Ivan B. Taylor, Detroit: As I said, there are three types of operations in which we used procaine, and we considered it only as an adjunct and not the chief anesthetic drug. The indication that we have used most of all was thoracic surgery. As Dr. Tuttle has pointed out, it has been found useful there, and we have about 200 cases done for Dr. Tuttle and his associates with this method. I should like to discuss more fully the anesthesia record of a first stage thoracoplasty. The patient was a woman about 35 years old. Thiopental sodium (450 mg.) was administered intravenously during induction, followed by nitrous oxide and intravenously administered procaine hydrochloride throughout the rest of the operation, which lasted less than an hour. This patient was not intubated for this

thoracoplasty. Her recovery was rapid. She was awake in five minutes, and that is not just active reflexes. The patient talked to us in five minutes and asked for fluid when she got back in the room. I told her she could have water and had a discussion with the special nurse because she had been nursing patients twenty years and "knew that they mustn't drink water after an operation." So I do not know whether it does much good to give good anesthesia; the attendants still want to treat the patients for poor anesthesia afterward. The patient had twenty minutes of complete relief from pain, was very comfortable and, of course, was able to clear out excess secretions by coughing. That is not an absolute indication, but it is one we have used most of all. For superficial operations, in which only light anesthesia is necessary, we have thought procaine was beneficial. These undesirable reflexes that we have encountered in anesthesia for years—excess salivation in light anesthesia, sweating which often occurs, cough, and so forth, things that occur in light anesthesia—have been fairly well depressed by the use of procaine hydrochloride in a 1 per cent solution. Some of these patients had as much as 2 or 3 Gm. of procaine an hour.

The patients undergoing thyroidectomy have done particularly well. Anesthesia for thyroidectomies is no longer the difficult problem that it was before the days when you didn't cool them off with propylthiouracil. I would like to try procaine on some patients with toxic thyroid disease.

PRESIDENT BISGARD: Dr. Granger?

DR. GRANGER: I have nothing to add.

POSTOPERATIVE MANAGEMENT OF PATIENTS UNDERGOING TRANSTHORACIC GASTROESOPHAGEAL OPERATIONS

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IT WAS not many years ago that a famous American surgeon made the statement that carcinoma of the esophagus is beyond the realm of surgical therapy. It is only in recent years that malignant lesions of the cardiac end of the stomach which have invaded the lower esophagus have been completely removed by operative means. The surgeon is indebted to the tremendous advances in anesthesiology and to progress in the field of antibiotics for his opportunity to attack such lesions. They have enabled him to open the chest and mediastinum, considerably diminishing the serious dangers with which he formerly was confronted. The availability of blood in quantities sufficient to replace losses as they are encountered diminishes the danger of hemorrhagic shock. Although these advances have made transthoracic procedures on the stomach and esophagus justifiable, such operations still carry a high mortality and morbidity. Several factors are contributory. Most patients who require this type of operation are old and debilitated and have lost from 30 to 50 pounds (13.6 to 22.7 Kg.) in weight. The reluctance of the patient to visit his physician early and of his physician to institute early surgical therapy generally results in a delay of many months between the onset of symptoms and the time of operation. This is reflected in the nutritional state of the patient, in his cardiac reserve and in his ability to withstand any extensive surgical procedure which carries with it much damage to tissues, considerable hemorrhage and loss of fluid, interference with

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From the Surgical Service, Veterans Administration Hospital, Hines, Ill., and the Department of Surgery, University of Illinois College of Medicine.

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respiration and shock. In spite of these factors, this type of operation offers many persons an opportunity for months or years of added life, comfort, and happiness, instead of an inevitable early death.

The greatest dangers of postoperative mortality in transthoracic gastroesophageal operations occur in the first few postoperative days. The mortality and morbidity are in direct proportion to the energy, efficiency and judgment displayed during their postoperative management. Best results are obtained by carefully planned team work of the surgeon, anesthesiologist, nurses and residents. At all times, the patient must be under the careful observation of a person who has knowledge of the postoperative routine and who can recognize the

TABLE 1.—*Relation of Type of Operation to Complications and Deaths* *

Type of Operation	No. of Cases	Complications*		
		None	Single	Multiple
Gastroesophageal resection	20	6	2	12 (5)
Exploratory thoracotomy	6	3	3 (1)	0

* The figures in parentheses indicate the number of deaths.

TABLE 2.—*Postoperative Complications*

Type	No.	Type	No.
Pulmonary		Cardiovascular	
Atelectasis	4	Cardiac failure	2
Edema	3	Thrombophlebitis	2
Bronchopneumonia	2		
Infarct	2	Miscellaneous	
Thoracic Cavity		Leakage at suture line	2
Hydrohemothorax	8	Subphrenic abscess	1
Empyema	2	Subcutaneous emphysema	1
Pneumothorax	1		
Hematoma of mediastinum	1		

early evidences of complications when they arise. A qualified surgical resident must literally "live with the patient" during the first few postoperative days. A delay in recognition and care of untoward symptoms frequently will result in the death of the patient.

Cardiovascular and respiratory complications are common and potentially serious. Similar complications have been reported by most surgeons performing these types of operations, regardless of the preoperative preparation or the surgical technic involved. The great majority of deaths occur in the early postoperative period.

At the Veterans Administration Hospital, Hines, Ill., 26 patients have been operated on for resection of the stomach and esophagus or of the esophagus alone through the transthoracic approach. As can be seen from table 1, resections were completed in 20 patients, of

whom 5 died postoperatively. The remaining 6 patients underwent exploratory thoracotomy, but the malignant lesions were so extensive that they were inoperable. Of this group 1 patient died. Of the entire 26 patients, 9 recovered without complications. Another 5 had only one major postoperative complication. The remaining 12 had multiple complications.

The various complications encountered and their frequency are listed in table 2.

Table 3 lists the time of death and the complications which developed in each of the fatal cases.

POSTOPERATIVE CARE

To minimize the frequency and severity of these complications, a plan of postoperative management has been developed and is employed.

TABLE 3.—*Factors Contributing to Postoperative Mortality*

Case	Esophageal Disease	Operation	P.O. Day of Death	Complications
1	Stricture	Resection	1	Atelectasis, bronchopneumonia, pulmonary edema, hydrohemothorax
2	Carcinoma	Thoracotomy	2	Massive pulmonary edema
3	Carcinoma	Resection	1	Cardiac failure
4	Carcinoma	Resection	2	Hydrohemothorax, hematoma of mediastinum
5	Carcinoma	Resection	2	Hydrohemothorax, cardiac failure
6	Carcinoma	Resection	11	Leakage at suture line, empyema, pulmonary infaret

It may be divided into eight cardinal points. These are: (1) stir-up regimen; (2) tracheobronchial toilet; (3) suction; (4) sedatives, narcotics and analgesics; (5) oxygen; (6) fluid and nutritional balance; (7) antibiotics, and (8) recovery routine.

Stir-Up Regimen.—We believe physical activity on the part of the patient to be one of the most important factors of the entire postoperative management. If this is neglected, disastrous results will likely occur. The regimen consists of five features.

(*a*) Deep Breathing: The patient is required to take six to ten deep breaths at least every half hour. This should repeatedly be observed by a competent member of the team and should be charted.

(*b*) Carbon Dioxide–Air Therapy: Many patients will not breathe deeply of their own accord. This group is forced to breathe deeply by the use of pure carbon dioxide–air which is administered in the following manner. A nozzle of the carbon dioxide tank is held approximately 8 to 10 inches (20 to 25 cm.) from the patient's face and the gas permitted to flow over the patient's face during eight to ten res-

pirations unless he manifests signs of increased respiratory exchange earlier. In this way adequate aeration is maintained in most of the alveoli of the lung. Air is advantageous because of its high nitrogen content, which is less rapidly absorbed from the alveoli. Thus, if the patient coughs, air will tend to force any secretions into the tracheobronchial tree, from which they can be coughed and expectorated.

(*c*) Frequent Turning from Side to Side: The patient should be requested to turn from side to side at least every half-hour. Too frequently patients are permitted to remain on their backs for long periods, encouraging stasis and resultant pulmonary complications. This activity likewise should be recorded on the chart, which should be carefully followed by the responsible physician.

(*d*) Coughing: Coughing should be encouraged to eliminate secretions from the tracheobronchial tree. Nothing should be done which will interfere with the cough reflex. This reflex serves as a "watchdog" of the tracheobronchial tree. Patients who do not cough because of pain can be given a paravertebral block and then encouraged to cough after the pain has been relieved. This activity must be insisted on, as most patients prefer to lie quietly and maintain shallow respirations. In case no secretions are present in the tracheobronchial tree, such activity is less important.

(*e*) Early Mobilization: It has been our policy to encourage the patient to move about as soon as possible. When expedient, he is asked to sit on the side of the bed on the second postoperative day and in a chair on the third. Because of the marked debility of most of these patients, we do not encourage walking in this early stage but do desire to have them in a sitting position.

Preoperative explanation of the importance of all of these factors to the patient elicits better cooperation on his part. Postoperative explanation is on occasion not productive of cooperation because of the toxic state of the patient.

Tracheobronchial Toilet.—We believe that the secretions in the tracheobronchial tree should be removed immediately. The presence of such secretions is considered a respiratory emergency, and they should be removed whenever noted, irrespective of the time of day or night. It is negligent to wait for signs of atelectasis or pneumonia before removing such secretions. Two methods are used to accomplish this. An endotracheal tube may be passed, under topical anesthesia, by visible or blind technic, and through this tube a suction catheter is passed. Daily roentgen and clinical observations serve as a guide to the bronchi needing aspiration. The vigorous coughing produced by the tube is an important factor in clearing the bronchi or in raising

the secretions to a level from which they can be aspirated. Where the endotracheal tube has not produced satisfactory removal of secretions, bronchoscopy is employed. It is also employed in case there is a specific obstruction of a branch bronchus with evidence of atelectasis. Prompt and frequent aspirations of the tracheobronchial tree should minimize the development of atelectasis.

Suction.—Gastrointestinal: A Rawson-Abbott tube is passed through the anastomosis at the time the stoma is made and is so anchored that the suction portion will remain in the stomach while the feeding limb extends into the duodenum or jejunum. We believe it important to keep the stomach deflated for the first four or five postoperative days to prevent this organ from becoming distended and causing tension on the suture line as well as compression of the lung. It also permits early postoperative feeding through the distal lumen. Gastric atony resulting from section of the vagus nerve as well as surgical manipulation almost invariably occurs and is followed by gastric distention if suction is not employed.

Thoracic: On completion of the gastrointestinal portion of the operation, a catheter is placed in the chest through a stab wound in an area best suited for dependant drainage. The lung then is fully expanded and kept so until the chest wall is closed, at which time the catheter is connected to a water trap. The maintenance of an efficient water seal is most important and demands frequent inspection. The minimal amount of pressure necessary to prevent the inflow of air during inspirations should be maintained. This usually requires from 3 to 5 cm. of negative pressure. The inevitable oozing of blood tends to produce clots which may block the catheter. To prevent this, the drain should frequently be stripped or irrigated with a solution of penicillin. If roentgen and physical examinations indicate that pneumothorax exists, expansion of the lung may be aided by the use of a Stedman pump in connection with the water seal. Maintenance of proper suction eliminates the hazards of pleural effusion, hydrothorax and hemothorax or pneumothorax. If proper suction is maintained, we have rarely had difficulty with pleural effusion. Occasionally blood or fluid will collect in the chest which cannot be removed through the existing catheter drainage. In these circumstances, the fluid is aspirated by a syringe and large needle. If the lung is well expanded and there is little or no fluid in the chest on the fourth or fifth day, the drain is removed. If fluid or air collects within the chest after removal of the drain, thoracentesis is immediately carried out and repeated whenever indicated.

Sedatives, Narcotics and Analgesics.—Our observations lead us to concur in the belief that patients who have had a transthoracic esophageal operation can be "killed with kindness." We are firmly convinced that only minimal amounts of sedatives, narcotics and analgesics should be used. During the first thirty-six postoperative hours, we administered from 50 to 100 mg. of meperidine hydrochloride (demerol hydrochloride®), as indicated. On the third postoperative day, it is rare that more than three doses of this drug are given. Opiates, barbiturates or drugs which tend to depress the cough reflex or respirations are avoided. If the patient complains of severe pain, we have relieved it by paravertebral block anesthesia. This in conjunction with small doses of demerol hydrochloride® has given satisfactory results.

Oxygen.—Oxygen is administered preferably by use of a BLB or similar mask with which some rebreathing takes place. This minimizes drying in the respiratory passages that frequently produces thick viscid secretions in the tracheobronchial tree which are difficult for the patient to eliminate. If a patient does not comfortably tolerate a mask, oxygen is administered by the oropharyngeal route. Oxygen tents are unsatisfactory, as they interfere with the care of these patients and the many inspections and examinations which are essential to the recognition of early complications. Such activities cannot be carried on in a tent if it is to maintain its most efficient function. Oxygen is used in the presence of tachycardia, tachypnea, cyanosis, early shock and evidences of inadequate respiratory exchange, such as atelectasis, secretions into the bronchial tree or pleural effusion. Although oxygen is not routinely used, we employ it at the slightest indication of hypoxia. Its main disadvantage is its dehydrating action on secretions in the tracheobronchial tree. Humidifiers have proved of little value to us in preventing this dehydration. Steam has the disadvantage of increasing the temperature, which, in turn, decreases the relative humidity.

Fluids and Nutritional Balance.—The maintenance of fluid balance is very important, but overhydration must be avoided because of the danger of pulmonary edema and an increased cardiac load. Isotonic sodium chloride solution should be used sparingly. We administer not more than 1,000 cc. on the first postoperative day and prefer to give only half that amount or less on subsequent days. Blood should be given to replace lost blood, but excessive amounts should be avoided. During the operation we administer from 1,000 to 3,000 cc. of blood, depending on the amount of bleeding encountered. Two intravenous setups with large needles are employed throughout the operation so that blood may be administered rapidly if vigorous bleeding is

encountered. In this manner, shock is avoided. The administration of whole blood and the amount employed in the postoperative period are determined by the amount of serosanguineous drainage from the pleural cavity and the clinical and laboratory indications of anemia. It is seldom if ever administered purely for its nutritional value, especially if the cardiac reserve of the patient is minimal.

The poor nutritional state of the great majority of these patients demands the early administration of food elements, particularly protein. A Rawson-Abbott tube permits the early drip feeding of solutions containing large amounts of proteins, carbohydrates and vitamins B, C and K. Such feedings are generally begun on the second or third postoperative day. Food elements which will coagulate or curd, such as milk, should be avoided, as they may be regurgitated into the stomach and block the holes on the suction portion of the Rawson-Abbott tube, with resultant gastric distention.

Antibiotics.—Antibiotics have been of inestimable value in the prevention of infection in patients undergoing transthoracic and mediastinal operations. However, we mention them far down on our list of cardinal points of postoperative care because their use does not replace or minimize the importance of the foregoing factors. Without proper attention to these factors, antibiotics will not prevent a high mortality. They can be relied on to retard the development of infection. Penicillin is given for several days preoperatively and postoperatively until the danger of infection is passed. This drug is administered intramuscularly and is used in solution for irrigation of the pleural cavity through the drainage catheter. Recently we have been using it by nasal inhalations in preoperative preparation. Streptomycin and sulfonamide drugs also are utilized when indicated.

Recovery Routine.—The establishment of a recovery room has greatly facilitated the postoperative care of all patients who have undergone major surgical procedures, particularly those having transthoracic operations. Both nursing and attending personnel have been trained and are familiar with all details of our postoperative regimen. The surgeon and the anesthesiologist are equally responsible for the care of the patient and work in harmony. They must be familiar with all details of postoperative therapy and must remain in constant attendance. Their diligence is the greatest factor in successful postoperative treatment.

SUMMARY

Transthoracic surgical procedures on the stomach and esophagus offer some measure of hope to many patients who, until recent years, were doomed to an early death from their disease or from starvation.

Although the incidence of cure of malignant diseases of these organs is not high, surgical intervention reestablishes continuity of the lumen of the gastrointestinal tract and permits these patients to eat food normally and to maintain their health and strength, often for many months or years. Because these patients are elderly and debilitated and in a poor nutritional state, and because the operation required to remove their disease is extensive, traumatic and shocking, the postoperative mortality will be high unless unusual care and diligence are exercised in their postoperative management. The factors which we believe to be important in postoperative therapy of patients who have undergone transthoracic esophageal operation are outlined and discussed.

GANGRENOUS PERFORATION OF THE GALLBLADDER

Analysis of Nineteen Cases

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IT IS NOW one hundred and five years since James Duncan,[1] surgeon at the Royal Infirmary in Edinburgh, cited a case of gangrene of the gallbladder with perforation, followed by peritonitis and death. The conditions were observed at autopsy. In 1894, fifty years following Duncan's observation, Hotchkiss[2] reported the first case in which operation was performed. In 1895, W. J. Mayo[3] reported the first successful removal of a gangrenous gallbladder. Since that time many reports have been published.

Gangrene of the wall of the gallbladder is complete necrosis of a portion of the wall in one or more areas. Gangrene of a portion of the gallbladder wall, followed by perforation, is a sequel of acute cholecystitis. The term does not imply that the entire gallbladder is gangrenous.

This report deals with 19 cases of gangrenous perforation of the gallbladder which fall into types 1 and 2 of the Niemeier[4] classification: acute free perforation and subacute pericholecystic abscess. Niemeier type 3, internal biliary fistula, is not included in this study.

INCIDENCE

This series of 19 gangrenous perforations of the gallbladder were found at operation (table 1). These cases extend over a period of twenty-one years (1928-1949), and the operations were done by sur-

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From the Departments of Surgery, St. Luke's Hospital and the University of Illinois College of Medicine.

1. Duncan, J.: Femoral Hernia: Gangrene of the Gall Bladder, Extravastion of the Bile, Peritonitis, Death, North J. Med. **2**:151-153, 1844-1845.

2. Hotchkiss, L. W.: Gangrenous Cholecystitis, Ann. Surg. **19**:197-205, 1894.

3. Mayo, W. J.: Some Observations on the Surgery of the Gall Bladder and Bile Ducts, Ann. Surg. **30**:452-458, 1899.

4. Niemeier, O. W.: Acute Free Perforation of the Gall Bladder, Ann. Surg. **99**:922-924 (June) 1934.

TABLE 1.—*Incidence of Perforated Gallbladders*

Author	Total Cases Reviewed	Total Cases of Acute Cholecystitis	No. of Cases with Perforation	% of Total Cases with Perforation	% of Acute Cases with Perforation	Mortality in Cases with Perforation
Fifield, L. R.: Brit. M. J. **2**: 635, 1926	1,066	153	28	2.6	....	43.0
Heuer, G. J.: Ann Surg. **99**: 881, 1934	800	106	23	2.8	21.0	34.7
Stone, W. W., and Douglas, F. M.: Am. J. Surg. **45**: 301, 1939	775	170	17	2.1	10.0	5.8
Mentzer, S. H.: Surg., Gynec. & Obst. **62**: 879, 1936	149	51	18	12.0	23.5	27.7
Edwards, C. R.; Gerwig, W. H., and Guyton, W. L.: Ann. Surg. **113**: 824, 1941	1,124	194	21	1.8	10.8	28.5
Wallace, R. H., and Allen, A. W.: Arch. Surg. **43**: 762 (Nov.) 1941	2,273	415	64	2.8	15.4	17.2
Diffenbaugh, Sarver and Strohl, 1949	1,127	75	19	1.6	25.3	21.5
Total	7,314	1,164	190	2.5	16.3	29.5

TABLE 2.—*Incidence of Perforations in All Types of Acute Cholecystitis as Collected from the Literature*

Author	Total No. of Cases of Acute Cholecystitis	No. of Cases with Perforation	% of Acute Cases with Perforation	Mortality in Cases with Perforation
Fifield, L. F.: Brit. M. J. **2**: 635, 1926	153	28	18.0	43.0
Graham, H. F.: Ann. Surg. **93**: 1152, 1931	198	10	5.0	5.0
Pratt, G. H.: Am. J. Surg. **22**: 46, 1933	120	3	2.5	33.3
Heuer, G. J.: Ann. Surg. **99**: 881, 1934	106	23	21.0	34.7
Mentzer, S. H.: Surg., Gynec. & Obst. **62**: 879, 1936	51	18	23.5	27.7
Heuer, G. J.: New York State J. Med. **36**: 1643, 1936	126	13	11.0	15.3
Pennoyer, G. P.: Ann. Surg. **107**: 543, 1938	300	61	20.3	13.1
Graham, H. F., and Hoefle, M. D.: Ann. Surg. **108**: 874, 1938	100	4	4.0	75.0
Totten, H. P.: Am. J. Surg. **41**: 29, 1938	100	20	20.0	10.0
Estes, W. L., Jr.: Am. J. Surg. **40**: 197, 1938	78	9	11.5	2.06
Stone, W. W., and Douglas, F. M.: Am. J. Surg. **45**: 301 1939	170	17	10.0	5.8
Hotz, R.: Am. J. Surg. **44**: 706, 1939	574	69	12.1	26.1
Koster, H., and Kasman, L. P.: Am. J. Digest Dis. **6**: 373, 1939	341	33	9.7	27.2
McCloskey, J. F., and Lehman, J. A.: Rev. Gastroenterol. **7**: 176, 1940	68	12	17.6	16.6
Atlee, J. L., and Atlee, J. L., Jr.: Pennsylvania M. J. **44**: 731, 1941	193	16	7.7	18.8
Frankel, H.; Abramson, E., and Berk, J. E.: Rev. Gastroenterol. **8**: 481, 1941	100	18	18.0	30.7
Edwards, C. R.; Gerwig, W. H., and Guyton, W. L.: Ann. Surg. **113**: 824, 1941	194	21	10.8	16.6
Wallace, R. H., and Allen, A. W.: Arch. Surg. **43**: 762 (Nov.) 1941	415	64	15.4	17.2
Glenn, F., and Moore, S. W.: Arch. Surg. **44**: 677 (April) 1942	350	25	7.1	12.0
McLanahan, S.; Trout, H., Jr., and Weary, W.: Am. J. Surg. **58**: 432, 1942	140	14	10.0	42.8
Schaeffer, R. L.: Pennsylvania M. J. **45**: 566, 1942	122	20	16.0	40.0
Hauk, G. W.: Pennsylvania M. J. **45**: 566, 1942	131	17	12.9	11.7
Wesson, H. R.: Proc. Staff Meet., Mayo Clin. **12**: 500, 1943	76	16	21.0	12.5
Blumberg, N., and Zisserman, L.: Am. J. Surg. **70**: 38, 1945	82	21	25.0	33.3
Bachhuber, C. A.; Deeb, P. H., and Taylor, E. A.: Am. J. Surg. **67**: 40, 1945	804	55	6.8	42.4
Johnstone, G. A., and Ostendorf, J. E.: Arch. Surg. **53**: 1 (July) 1946	105	3	2.8	0
Diffenbaugh, Sarver and Strohl (1949)	75	19	25.3	21.5
Totals	5,272	630	11.9	23.8

geons of one service at St. Luke's Hospital. During these twenty-one years, there were 1,127 operations on the gallbladder, with 19 cases of Niemeier's types 1 and 2 perforations. This is an incidence of 1.69 per cent. Of these 1,127 operations, 75, or 6.65 per cent, were for acute cholecystitis. By acute cholecystitis we mean pathologically confirmed acute inflammation of the gallbladder wall. An extensive review of the literature reveals perforations in 11.9 per cent of 5,272 cases of acute cholecystitis. The mortality rate following perforation in this collected series of acute cholecystitis was 23.8 per cent (table 2). The incidence of 25.33 per cent of perforations in pathologically confirmed acute cholecystitis at St. Luke's Hospital, Chicago, prompted this study.

AGE

The youngest patient was a man aged 29; the oldest, a woman aged 79 (table 3). The average age of the 10 women was 58.6 years and

TABLE 3.—*Age Incidence*

Age, Yr.	Cases, No.	Percentage
20-29	1	5.2
30-39	4	21
40-49	1	5.2
50-59	4	21
60-69	2	10.5
70-79	7	37

of the 9 men 56.0 years. The average age of the total group was 57.2 years. Four patients, or 21 per cent, were between 30 and 39 years of age, and 13, or 68.5 per cent, were over 50.

SEX

Ten, or 52.6 per cent, of the patients were women, and 9, or 47.3 per cent, were men. Of the 13 patients past 50 years of age, 6 were men and 7 were women.

DURATION OF PRESENT ILLNESS

Sixteen perforations of the gallbladder, or 84 per cent, occurred between twelve and seventy-two hours after the onset of symptoms (table 4). In 3 cases, or 16 per cent, the present illness extended over a three to six day period. In Cowley and Harkins'[5] series of 25 cases, 9 perforations, or 36 per cent, occurred within the first thirty-six hours.

5. Cowley, L. L., and Harkins, H. N.: Perforation of the Gall Bladder, Surg., Gynec. & Obst. **77**:661-668 (Dec.) 1943.

DURATION OF HISTORY OF PREVIOUS ATTACKS

Sixteen patients, or 84 per cent, gave a history of previous disease of the gallbladder. In 11 patients, or 57.8 per cent, the disease extended over a period of from two to more than ten years. It is interesting to note that in 3 cases, or 16 per cent, no history of previous disease of the gallbladder was obtained.

SYMPTOMS

Pain in the right upper abdominal quadrant was present in all 19 cases (table 5). Nausea was present in 11 cases and vomiting in 10. In 3 cases there was generalized abdominal pain. Chills and fever

TABLE 4.—*Duration of Present Illness*

Duration of Illness, Hr.	Cases, No.	Percentage
12-24	9	47
24-72	7	37
72-144	3	16

TABLE 5.—*Symptoms*

Symptoms	Cases	
	No.	%
Pain in right upper quadrant	19	100
Nausea	11	60
Vomiting	10	58
Generalized abdominal pain	3	16
Chills and fever	3	16

were present in 3 cases; at operation, in these 3 cases stones were found in the common duct.

LABORATORY DATA

The leukocyte count was of little significance in demonstrating the presence of perforation of the gallbladder. In 9 cases (47 per cent) the leukocytes numbered more than 20,000; in 3 cases (16 per cent) they ranged between 10,000 and 15,000, in 4 (21 per cent) between 6,000 and 10,000 and in 3 between 15,000 and 20,000.

TEMPERATURE

Fifteen patients, or 78.9 per cent, had rectal temperatures between 101.6 and 103 F. Two patients, or 10.5 per cent, had rectal temperatures of 98.6 and 100 F.; 1 or 5.2 per cent, of from 100 to 101.6 F. and 1 above 103 F.

PHYSICAL FINDINGS

Tenderness in the right upper abdominal quadrant was present in all 19 cases (table 6); a mass was palpable in 10 (58 per cent) and jaundice was present in 4 (21 per cent).

PREOPERATIVE DIAGNOSIS

In 13 cases, or 70 per cent, the diagnosis of perforation of the gallbladder was made preoperatively. It should be pointed out again that these 19 cases were from the same surgical service; there have been continuity and overlapping of attending surgeons throughout the years

TABLE 6.—*Physical Findings*

Physical Findings	Cases	
	No.	%
Tenderness in right upper quadrant	19	100
Mass in right upper quadrant	10	58
Jaundice	4	21
Shock	1	5

TABLE 7.—*Grouping According to Niemeier Classification*

Classification	Cases		Deaths,	Mortality,
	No.	%	No.	%
Type 1, acute free perforation	7	35.0	2	29.0
Type 2, pericholecystic abscess	12	60.0	2	17.0
Total	19	....	4	Over-all Mortality, 21%

covered by this study, and consultations among the members of this service are frequent.

GROUPING ACCORDING TO NIEMEIER CLASSIFICATION

In 7 cases, or 35 per cent, the perforations were of the Niemeier type 1, or acute free perforations (table 7). There were 2 deaths in this group, a mortality rate of 29 per cent. In 12 cases, or 60 per cent, the perforations were of the Niemeier type 2, or pericholecystic abscess. There were 2 deaths in this group, a mortality rate of 17 per cent. Four deaths in 19 cases represents an over-all mortality rate of 21.5 per cent.

TYPE OF OPERATION

In 11 cases, or 57.8 per cent, the gallbladder was removed (table 8). On 2 occasions stones were found in the common duct, and drain-

age of the common duct was instituted at the time of cholecystectomy. On 1 occasion the appendix was removed at the time of cholecystectomy.

In 8 cases, or 42 per cent, drainage of the gallbladder was carried out. On 1 occasion, stones were found in the common duct, and drainage of the common duct was done at the time of cholecystostomy.

LENGTH OF STAY IN THE HOSPITAL

The average stay in the hospital of the 15 patients who recovered was 31.5 days.

ANALYSIS OF THE DEATHS

Three of the 4 deaths in this series were due to sepsis and peritonitis.

One patient, a 35 year old woman, died on the forty-seventh postoperative day. The duration of symptoms before operation in this case was twenty-four

TABLE 8.—*Type of Operation*

Type of Operation	Cases	
	No.	%
Cholecystectomy	8	42.0
Cholecystectomy and choledochotomy	2	10.5
Cholecystectomy and appendectomy	1	5.2
Cholecystostomy	7	37.0
Cholecystostomy and choledochotomy	1	5.2

hours. Drainage of the gallbladder had been performed elsewhere three months previously. At autopsy there were many intra-abdominal abscesses, cholangitis, abscesses of the abdominal wall and abscesses of the right breast.

A 71 year old man died suddenly on the fifth postoperative day. The duration of symptoms in this case was forty-eight hours. He gave no history of previous gallbladder disease. Autopsy was not done. The clinical diagnosis of the cause of death was coronary occlusion.

A 55 year old woman died on the second postoperative day. Operation revealed a gangrenous perforation with pericholecystic abscess, free bile in the peritoneal cavity and stones in the common duct. Peritonitis was given as the cause of death.

A 56 year old woman, with severe diabetes mellitus, died twenty-four hours postoperatively. Her temperature rose to 106 F. and the pulse rate to 160. The diabetes had been poorly controlled for several days prior to her admission to the hospital. She gave a history of known gallbladder disease, with intermittent chills and fever, of one year's duration. At operation the gallbladder and an abscess were drained. Free bile and pus were found in the abdomen. Peritonitis was given as the cause of death.

All deaths occurred prior to the use of chemotherapeutic agents or antibiotic drugs in this hospital.

COMMENT

Gangrenous perforations of the gallbladder are not infrequent abdominal emergencies. The mortality rate of 21.5 per cent in this series and 23.8 per cent in a series of 630 perforations collected from the literature emphasizes the seriousness of the condition.

Eliason and McLaughlin [6] stated that "a correct diagnosis of a perforated gallbladder is quite unusual." This statement is corroborated by Sanders [7] who reported a correct diagnosis in 4 of 46 cases. Cowley and Harkins [5] reported a correct diagnosis in 3 of 25 cases. From our study, we note that there is little on which to base a diagnosis of impending perforation. Furthermore, tenderness, pain and a palpable mass in the upper part of the abdomen are common conditions in many cases of acute cholecystitis.

In this series, the disease seemed progressive, which is a helpful factor in the differential diagnosis. We believe that frequent observations of the patient and his progress are of major importance in the proper evaluation of major abdominal emergencies. A careful history, accurate physical examination and evaluation of laboratory data in terms of the clinical picture, with an appreciation of the frequency with which gallbladders perforate, should lead to a greater number of correct diagnoses.

SUMMARY AND CONCLUSIONS

A series of 19 cases of gangrenous perforation of the gallbladder is reviewed. The cases occurred during a twenty-one year period, 1928 to 1949. During this period a total of 1,127 operations on the gallbladder were performed. In 75 cases, pathologically confirmed acute cholecystitis was present. The incidence of perforated gallbladders occurring in patients undergoing all types of operations on the gallbladder in this series was 1.69 per cent. The incidence of perforated gallbladders in patients with acute cholecystitis was 25.33 per cent.

Of the 19 perforated gallbladders, 7 were of the Niemeier type 1, acute free perforation. Twelve perforations were associated with pericholecystic abscesses, Niemeier type 2.

Four deaths occurred in the 19 cases reported, a mortality rate of 21.5 per cent.

There were no distinctive signs, symptoms or laboratory findings to establish the diagnosis of impending or actual perforation of the gallbladder. Localized pain and tenderness in the right upper quadrant,

6. Eliason, E. L., and McLaughlin, C.: Perforation of the Gall Bladder, Ann. Surg. **99**:914-921 (June) 1934.

7. Sanders, R. L.: Perforations of the Gall Bladder; Analysis of Forty-Six Cases, Surgery **1**:949-958 (June) 1937.

with the presence of a localized mass, associated with clinical and laboratory evidence of persistence or progression of the process, indicated the diagnosis in most instances.

Analysis of the 4 deaths revealed that 3 resulted from progression of sepsis secondary to the perforation. The remaining death followed an acute coronary occlusion on the fifth postoperative day.

In 16 cases, or 84 per cent, perforation of the gallbladder occurred in eighteen to seventy-two hours after the onset of symptoms.

Symptoms of previous gallbladder disease were present in 16 cases, or 84 per cent.

In view of the frequency of gangrenous perforation in acute cholecystitis (25.3 per cent) and the high mortality of gangrenous perforation (21.5 per cent), we conclude that operation should be done when there is evidence of progression of the disease during the first forty-eight hours following the onset of symptoms.

ADEQUATE SUBTOTAL GASTRIC RESECTION FOR DUODENAL ULCER

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AND
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THE LITERATURE since 1946 has abounded with reports and discussions concerning the merits and complications of vagotomy for duodenal ulcer. We do not propose to present definite opinions regarding the procedure, since we have had no experience with the operation. The summaries and conclusions reached by others are available to all for study, and, since the majority of investigators have reported favorably, we who have resorted exclusively to subtotal resection must pause and carefully consider the longer term results of the latter operation.

Visick,[1] of England, in reporting 505 resections for peptic ulcer, of which 357 were for duodenal ulcer, has stated that "only by carefully following all patients and assessing their condition by independent tribunal can we gain a true picture of the effectiveness of any procedure."

Crile [2] has pointed out that the results of resection have left much to be desired. Extensive resections are often followed by inability to gain weight or by the dumping syndrome. Less radical resection may be followed by marginal ulcer in up to 6 per cent of cases. Contrariwise, vagotomy as reported in other series has been followed by such untoward symptoms as retention, diarrhea, bloating, belching of foul gas, nausea and weakness. Recurrence of the ulcer has also been reported.

Our series of resections is small, for we feel, as did Jordan,[3] that radical surgical intervention, even if productive of good results, should be done only with impelling indications. One wonders when studying the reports of large series of vagotomies whether the indications have been as definite in all cases. The relative ease of performance of the

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From The Department of Surgery, Duluth Clinic.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 19, 1949.

1. Visick, A. H.: Lancet **1**:505-544 (April 3) 1948.
2. Crile, G., Jr.: S. Clin. North America **28**:1123 (Oct.) 1948.
3. Jordan, S.: End Results of Radical Surgery of Gastrointestinal Tract as Seen by Gastroenterologist, J. A. M. A. **116**:586-590 (Feb. 15) 1941.

operation and the lessened mortality rate might induce patients with mild complications to accept vagotomy earlier in the course of their disease, whereas many hesitate to submit to resection until their discomfort drives them to seek any relief offered. Our discussion, then, concerns itself solely with those patients who have had resection for real complications and seeks to answer two questions: 1. Is the patient free of his disease? 2. Is the patient comfortable.

In the past five years we have performed resection for benign peptic ulcer in 201 cases, of which 121 were cases of duodenal ulcer. The ratio of male to female patients is about 5.3 to 1 as is shown in table 1. The average age at operation is about equal in the two sexes.

TABLE 1.—*Sex and Age*

Sex	Number of Patients	Average Age in Years
Male	102	45.6
Female	19	42.1
Total	121	

TABLE 2.—*Previous Operations*

Operation	Number of Operations
Acute perforation	15 (1 marginal ulcer)
Gastroenterostomy	6
Pyloroplasty	6
Exploratory	2
Gastric resection	1
Billroth no. 1	1
Vagotomy	1
Total	32*

* 32 operations in 28 patients, or 23 per cent of patients.

Twenty-eight patients, or 23 per cent of the series, had had previous operations, as is noted in table 2. The majority of these operations were for closure of an acute perforation, with gastroenterostomy and pyloroplasty next in frequency. Vagotomy had been performed in 1 instance, this operation having been done elsewhere.

All our patients have been thoroughly studied by the department of internal medicine prior to operation, and all have been given adequate trials of conservative therapy. The indications for operation have been persistent and severe pain, obstruction and hemorrhage or any combination of these three, all unrelieved by adequate and careful medical therapy. All cases, therefore, represent the real complications of duodenal ulcer, and the average duration of symptoms has been many

years. Table 3 shows that pain was present in 98 patients, hemorrhage in 27 and obstruction in 30. In many patients more than one sypmtom was present. The average duration of symptoms was about 11.4 years. In 1 patient, symptoms had been present for thirty-three years.

Our concept of adequate gastric resection is not new. We attempt to remove the ulcer, or, when this is unduly hazardous—as when an ulcer lies in close proximity to the common duct or is involved in a great deal of scar tissue—to exclude it. We resect at least two thirds to three fourths of the stomach, including the lesser curvature up to the esophagus, or as near thereto as possible, and perform retrocolic or antecolic gastrojejunostomy, using a short proximal jejunal loop. The anastomosis is of the open type and is followed by thorough peritoneal toilet. With the routine preoperative use of succinylsulfathiazole (sulfasuxadine®), phthalylsulfathiazole (sulfathalidine®) or phthalylsulfacetimide (thalamyd®) and gastric lavage, we have not had cause

TABLE 3.—*Symptoms* and Average Duration in Years*

Symptom	No. of Cases
Pain	98
Hemorrhage	27
Obstruction	30
Average duration in years	11.4

* In many cases, more than one symptom was present.

to abandon the open operation. Recently penicillin has been administered to the patients for one or two days preoperatively. An indwelling nasal suction tube is always pulled through the anastomosis and placed well within the proximal jejunal loop and, thence, into the duodenum. Since we have added this protection to closure of the duodenal stump with silk sutures, blowout has not occurred. Buttressing of the duodenal stump against the pancreas has been abandoned. In 1943 and 1944, the anterior Polya operation was done in the majority of cases. Since 1944, the Hofmeister procedure has been the operation of choice. It should be mentioned that the Finsterer exclusion procedure with excision of the antral mucosa was done in 11 cases but has not been performed since September 1946.

The immediate postoperative complications which developed in 20 cases, or 16 per cent, are shown in table 4. These represent all the postoperative complications in the series and, for the most part, are relatively minor. Under pulmonary complications we have grouped atelectasis and pleurisy. The wound infections have, for the most part, been trivial infections of the nature of minor stitch abscesses, except

for 1 case in which evisceration occurred. Prompt secondary closure in this patient resulted in recovery without further incident. Two patients required reoperation because of stomal obstruction and retention, and it is of interest to note that in both cases the closed anastomosis had been done; the last such case occurred in 1945.

There were 7 deaths in the entire series of 201 cases, or a mortality rate of 3.4 per cent. In the group with duodenal ulcer there were 6 deaths, 3 of which we feel were not directly attributable to surgical error.

TABLE 4.—*Immediate Postoperative Complications*

Complication	Number of Cases
Pulmonary	6
Wound infection	6
Retention	2
Hemorrhage	2
Subphrenic abscess	2
Pelvic peritonitis	1
Intestinal obstruction	1
Total	20 (16% of cases)

TABLE 5.—*Postoperative Deaths and Causes*

Case No.	Cause	Interval, Days	Autopsy
1	Peritonitis (3 previous operations on stomach)	1½	Yes
2	Duodenal leak; hemorrhage	18	Yes
3	Perforation at anastomotic line; hemorrhage	21	Yes
4	Psychosis; acute depression	8	Yes; autopsy did not show cause of death
5	Pulmonary embolus	9	Yes
6	Uremia (clinical)	12	No

Table 5 lists the causes of death. The mortality rate in the series with duodenal ulcer is, thus, 4.9 per cent; excluding the last 3 cases, the rate is reduced to 2.4 per cent. In cases 2 and 3 faulty suture technic was probably to blame for the fatalities. Case 4 was that of a woman who, in a period of very acute depression predicted her own death. Death occurred on the eighth postoperative day, but autopsy did not show the cause of death. The peritoneal cavity was clean, and all the suture lines were completely intact. In case 5, sudden death occurred as a result of pulmonary embolus on the day of the patient's anticipated discharge from the hospital. Since August 1947, 74 consecutive resections for peptic ulcer have been performed without fatality and with only 1 serious complication.

Some months ago in an attempt to evaluate our results, we sent a questionnaire to all patients subjected to resection for duodenal ulcer since January 1943. Six cases have been lost to follow-up through postoperative deaths. Five cases have been lost through late deaths, three to five years after operation, but in no instance was the death in any way related to the gastrectomy. In 10 cases there has been no reply to the questionnaire. Returns have been secured in 100 cases, or 90 per cent; these 100 cases furnish the material for this report.

A reproduction of the questionnaire which was sent out accompanies this article. By means of it, we attempt to enumerate the commoner postgastrectomy symptoms to permit the patient to evaluate his own personal result on the basis of the questions listed. Our patients are seen postoperatively at one month intervals for six months and twice a year thereafter. At each office visit, the patient's status is evaluated by the surgeon and the internist. Gastrointestinal roentgen study is performed in the majority of instances, usually within six months after

TABLE 6.—*Cases Available for Study*

Total operations		121
Postoperative deaths	6	
Late deaths	5	
Lost to follow-up	10	
Total not followed	21	
Available for follow-up		100

the operation. While the degree of acidity is not measured in all cases postoperatively, about one half the patients have had test meal studies, and in only 1 instance has achlorhydria been absent. All patients are routinely placed on a rather restricted diet for six to eight weeks. Thereafter they are instructed to eat whatever foods they desire. If any food causes distress, we merely advise the patient to eliminate that item from his diet. Foods not tolerated well appear to be fried or spicy foods, chocolate, pork, cabbage, onions and coffee. Alcohol and tobacco in moderation are not forbidden. We have felt that, in addition to the regular follow-up, an analysis of the patient's answer to the questions enumerated in the questionnaire, plus giving the patients themselves an opportunity carefully to evaluate their status, would enable us to assess the result with a good degree of accuracy in almost every instance. We have not changed the evaluation placed on his result by any patient, even though symptoms listed by him may have been very vague or mild.

Uniformly, the highest percentage of excellent or good results was obtained in that group subjected to resection because of obstruction with or without pain. In 30 such cases the results were excellent or good,

except in 1 instance in which the result was evaluated by the patient himself as only fair. There were no poor results in this group.

Less satisfactory results were apparent in the group offering intractable pain or pain with hemorrhage as the operative indication. Of 70 patients in this group, 13, or 18 per cent, had fair or poor results. It would seem from an analysis of other studies that in this group

TABLE 7.—*Results According to Operative Indication*

Indication	Result		
	Excellent or Good	Fair	Poor
Obstruction with or without pain	29	1	0
Pain alone or with hemorrhage	57	8	5
Total	86	9	5

Questionnaire

1. Are you able to eat any and all foods?
   Yes..... No.....
2. If some foods cause you distress, indicate which foods.....
3. Do you have any of the following stomach symptoms? Check which ones.
   a. Pain..... After meals.....
   b. Vomiting.....
   c. Nausea.....
   d. Bleeding.....
   e. Feeling of fullness.....
   f. Belching.....
   g. Diarrhea.....
   h. Constipation.....
   i. Loss of appetite.....
   j. Any others.....
4. Have you returned to work?.....
5. Can you do a full days work?.....
6. Present weight.....
7. Do you think your result from operation is
   a. Excellent.....
   b. Good.....
   c. Fair.....
   d. Poor.....

vagotomy may prove to be a better procedure. In many of these cases, however, we found subacute or chronic perforation of a posterior ulcer into the pancreas, and one wonders whether any operation short of actual excision or exclusion of the ulcer will result in permanent cure.

Table 8 shows the end results as evaluated by the patient's own answers to the questionnaire. It will be seen that 86 per cent had excellent or good results; 9 per cent, fair, and only 5 per cent have reported a poor result.

The so-called "dumping syndrome" has occurred to our knowledge in only 3 patients, and of these, 2 have experienced relief over periods of from one to four years. Nausea alone has occurred in about 8 per cent of cases, this varying from very mild occasional nausea to a somewhat more distressing and permanent symptom. Nausea and vomiting together have occurred in about 8 per cent of cases, and here again

TABLE 8.—*Results in 100 Cases with Follow-up*

Result	Number of Cases	Percentage of Cases
Excellent or good	86	86
Fair	9	9
Poor	5	5
Total	100	100

TABLE 9.—*Occurrence of Postgastrectomy Symptoms*

Symptom	Number of Cases	Percentage of Cases
"Dumping"	3	3
Nausea alone	8	8
Nausea and vomiting	8	8
Marginal ulcer *	1	1
Failure to gain weight	10	10

* The patient claims an excellent result, but a roentgenogram reveals a questionable marginal ulcer. This is the only patient in the series with high free hydrochloric acid level postoperatively.

TABLE 10.—*Results According to Type of Operation*

	Polya		Hofmeister	
Result	Number of Cases	Percentage of Cases	Number of Cases	Percentage of Cases
Excellent or good	24	86	62	86
Fair	2	7	7	10
Poor	2	7	3	5

the symptoms, for the most part, have been transient and rather vague. Marginal (stomal) ulcer is thought to be present in only 1 case, and here the only evidence is a questionable roentgen defect of the stoma; the patient himself has only minor complaints. Of the cases with postoperative test meal studies, this is the 1 case in which achlorhydria was not produced. Failure to gain weight has occurred in 10 per cent of the cases.

Table 10 shows the results according to the type of operation, and our figures seem to indicate that the type of operation makes little difference as to end results provided an adequate resection is performed.

SUMMARY

One hundred and twenty-one cases of adequate gastric resection for chronic, complicated duodenal ulcer are reported.

A mortality rate of 4.9 per cent would appear to be unduly high, but eliminating 3 cases in which death was not felt due to error in surgical technic, the rate becomes 2.4 per cent. Postoperative complications occurred in 16 per cent.

Excellent and good results have been secured in 86 per cent of cases, the fair or poor results occurring in that group of patients subjected to resection for persistent pain or pain with hemorrhage. In 1 case, gastrointestinal roentgen studies suggests marginal (stomal) ulcer; the patient has only minor complaints not at all suggestive of marginal ulcer.

Distressing postgastrectomy symptoms have occurred in a small percentage of patients; in many of these, symptoms have abated over a period of years.

VON HABERER-FINNEY GASTRECTOMY WITH VAGOTOMY

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WHEN BILLROTH performed the first successful partial gastrectomy in 1881, he restored intestinal continuity by anastomosing the stump of the stomach to the end of the duodenum. He was, indeed, the father of gastric surgery; for all thirty-seven different methods (Polya [1]) of reestablishing the gastrointestinal tract after partial removal of the stomach are modifications either of his original operation, gastroduodenostomy (Billroth I), or his subsequent procedure, gastrojejunostomy (Billroth II, 1885). Contemporaries of Billroth followed his first technic or devised modifications of their own, but modern gastric surgeons have tended to practice some variation of the Billroth II operation. The swing away from gastroduodenostomy to gastrojejunostomy occurred because the latter proved to be a safer operation. The difficulty in end to end anastomosis of the stomach and duodenum is due chiefly to inequality in size of the openings. That this was a real problem in the early days of gastrointestinal surgery is evidenced by the many modifications advocated and by constant reference in the surgical literature of that period to the dangerous upper angle, or "angle of sorrows."

The large number of marginal, or jejunal, ulcerations that followed short circuiting in the treatment of complicated duodenal ulcers led to the abandonment of this type of operation. Substitution of partial or subtotal gastrectomy has reduced the number of marginal ulcers, but the incidence is still high. Over the years many surgeons have reverted to the Billroth I type of operation on the ground that it is more physiologic and that the duodenum is better endowed by nature to withstand the often undiluted acid gastric secretions. Schoemaker was one of the first to free himself from the Billroth I prejudice.[2] He

From the Department of Surgery, the Henry Ford Hospital.

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1. Polya, E.: Re-Establishment of the Gastro-Intestinal Passage after Gastric Resection, Surg., Gynec. & Obst. **70**:270-290, 1940.

2. (*a*) Mayo, W. J.: Radical Operations on the Stomach with Especial Reference to Mobilization of the Lesser Curvature, Surg., Gynec. & Obst. **36**:447-453, 1923. (*b*) Schoemaker, J.: Zur Technik der Magenresektion nach Billroth I, Arch. f. klin. Chir. **121**:268-271, 1922.

recognized that the fatal suture angle could be avoided by improved technic. His contribution was the discovery that by removing all the lesser curvature, and thereby tubing the stomach, secure anastomosis could be made since tension was eliminated, and the size of the end of the stomach was reduced. Likewise W. J. Mayo [2a] showed that ligation of the left gastric artery near its origin added appreciably to the mobility of the stomach. Moreover, Polya [1] in spite of introducing the universally accepted modification of the Billroth II operation (1910), which bears his name, actually favors gastroduodenostomy.

The modern modification of the Billroth I technic as sponsored by Clagett and Waugh,[3] of the Mayo Clinic, and others is not easily applicable to many cases of penetrating heavily scarred duodenal ulcers on account of the difficulties and dangers inherent in mobilizing sufficient of the end of the duodenum to effect direct anastomosis. The situation may be met by utilizing the modification introduced by von Haberer [4] in 1922 and Finney [5] in 1923. Essentially, this consists in closing the end of the duodenum and anastomosing the end of the stomach to the side of the mobilized descending duodenum, terminolateral gastroduodenostomy. Since the von Haberer-Finney modification was presented, numerous references have been made to this procedure in literature, but we have been unable to find any sizable series of case reports.

RATIONALE

The following advantages of gastroduodenostomy may be cited:

1. *Anatomic.*—The normal anatomic relationship is restored.

2. *Physiologic.*—Gastric contents after operation are poured into the duodenum, an organ accustomed to receiving acid secretion and, theoretically at least, better adapted for this purpose than the jejunum.

3. *Technical.*—(*a*) The entire operation is performed in the supracolic compartment, a fact of definite value when dealing with substandard patients and when the procedure must be carried out under local anesthesia, since disturbance of the colon, mesocolon and small intestine is avoided. (*b*) The duodenal stump should be more secure, since back pressure on this area is impossible. (*c*) Postoperative gastric retention due to mechanical kinking at the stoma does not occur.

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3. Clagett, O. T., and Waugh, J. M.: Indications for and Advantages of Schoemaker-Billroth I Gastric Resection, Arch. Surg. **56**:758-765 (June) 1948. Higginson, J. F., and Clagett, P. T.: The Schoemaker-Billroth I Operation, Surgery **24**:613-620, 1948.

4. von Haberer, T.: Terminolaterale Gastroduodenostomie ober der Resektionsmethode nach Billroth I, Zentralbl. f. Chir. **49**:1321-1326, 1922.

5. Finney, J. M. T.: A New Method of Gastroduodenostomy, End to Side, with illustrations, Tr. South. S. A. **36**:5 and 76, 1924.

The following objections have been raised: 1. The operation technically is more difficult than gastrojejunostomy. 2. Insufficient stomach is resected. This objection is invalidated if the duodenum and stomach are adequately mobilized and the decision to utilize the operation is not made until after the resection is accomplished. 3. Reflux of beneficial alkaline duodenal contents into the stomach is less than after gastrojejunostomy. Continuous postoperative gastric aspiration in comparable groups of patients has shown that there is no appreciable difference in the amount of duodenal contents removed. 4. Complete mobilization of the duodenum increases the tendency to duodenal ileus. This did not occur in any of our patients.

PERSONAL EXPERIENCE

An encouraging experience with the von Haberer-Finney gastrectomy in the treatment of jejunal ulcer prompted the use of the technic in gastric ulcer and an occasional early case of gastric carcinoma with gratifying results. Since early in 1946 we have performed subtotal gastrectomy plus vagotomy on practically all patients with duodenal ulcer. This additional procedure appears to be satisfactory, as well as we can judge, for in none of these patients has a jejunal ulcer developed, a statement we could not make regarding any other three year period when subtotal gastrectomy alone was done. Difficulty with gastric retention following vagotomy led us to substitute the duodenum for the jejunum in restoring continuity, and again the result justified continuance of the method. We have now used the operation in 50 cases during 1947 and 1948, but these were not consecutive gastrectomies, since the method is not applicable to all cases. Among the patient's there were 42 with duodenal ulcer, of whom 20 had one or more episodes of hemorrhage, 9 had had perforation and in 25 some degree of obstruction was present. Delayed emptying of the stomach in spite of the concomitant vagotomy was not a problem in any of these patients, and neither the dumping syndrome nor recurrent ulcer has been observed. There was 1 death in the series attributed to hepatic failure on the basis of observations at autopsy, which also showed that the anastomotic suture lines were intact. The closed duodenal stumps and the anastomoses all healed without leakage. Appraisal of end results in the 46 patients who were followed after operation indicated good results in 39 (84.7 per cent) and fair in 7 (15.3 per cent). In other words, the end results were about the same as for a comparable group in which restoration of continuity was established by gastrojejunostomy.

OPERATIVE PROCEDURE

1. *Mobilization of the Duodenum.*—The peritoneum and fascia propria lateral to the descending duodenum are sectioned (fig. 1 *A*), thereby mobilizing both the duodenum and the head of the pancreas

(fig. 1 *B*). This exceedingly useful maneuver [6] not only permits adequate inspection and palpation of these organs to determine the feasibility of resection in penetrating duodenal ulcers complicated by edema and induration but also facilitates closure of the duodenal stump.

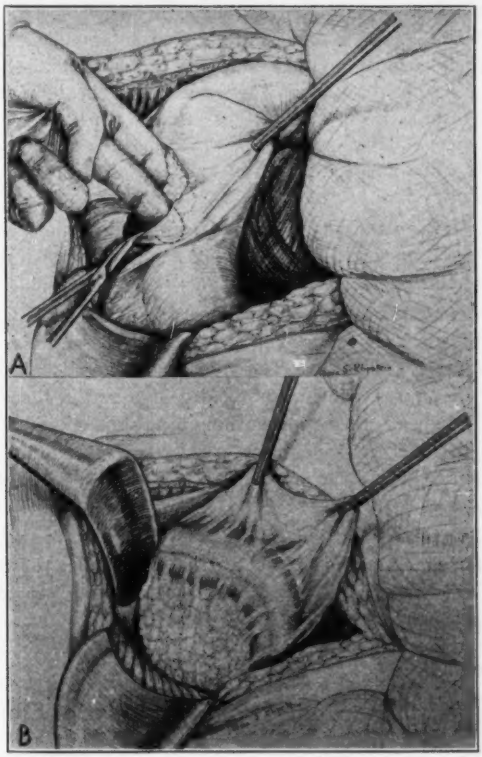

Fig. 1.—*A*, method of mobilizing the duodenum and head of the pancreas. The peritoneum is incised, and then the fascia propria is divided. *B*, completed mobilization of the duodenum and head of the pancreas. This drawing overemphasizes the amount of the peritoneum present.

2. *Ligation of the Left Gastroepiploic Artery.*—The watershed between the right and left gastroepiploic arteries is defined, and the left artery is clamped and tied. Frequently this consists in tying only a

6. (*a*) Finney, J. M. T., Jr.: Pyloroplasty and Gastroduodenostomy, Surgery **2**:738-758, 1937. (*b*) Wilkie, D. P. D.: Some Principles in Abdominal Surgery, Surg., Gynec. & Obst. **50**:129-138, 1930.

slender communicating branch, for in most instances the anastomoses between these two vessels takes place in the gastric wall rather than in the gastrocolic omentum. The last two radicles of the left gastroepiploic artery are then ligated between the greater curvature and the artery to allow a higher removal of stomach.

3. *Ligation of the Right Gastroepiploic Artery.*—This artery is picked up and ligated in the gastrocolic omentum about 2½ inches (6 cm.) proximal to the pylorus so as not to denude entirely the great omentum of its blood supply. The gastrocolic omentum between the two ligated arteries is cut and tied, as are the primary radicles of the right gastroepiploic artery going to the pylorus and prepyloric region of the stomach. The middle colic artery must be identified and protected during this procedure.

4. *Ligation of the Right Gastric Artery.*—The right gastric artery now is double clamped and ligated (fig. 2), thereby completing mobilization of the pyloric end of the stomach.

5. *Sectioning and Closing the Duodenum.*—A small Payr clamp is put on the stomach just proximal to the pylorus and the duodenum cut across just distal to it. The duodenal stump is closed with a double row of sutures, and the suture line is buried in the head of the pancreas. In difficult cases of penetrating ulcer, it is advisable not to use a clamp on the duodenal side, since every bit of tissue may be needed for the closure.

6. *Ligation of the Left Gastric Vessels.*—The left gastric artery and vein are identified by turning the stomach over to the left and are isolated, clamped, cut and ligated at a point proximal to the first gastric branch (fig. 2). The gastropancreatic omentum is sectioned with the vessels, thereby removing the main support of the stomach [2] and producing maximum mobility of the organ.

7. *Section of the Vagus Nerves.*—Upward retraction of the left lobe of the liver and downward retraction of the mobilized stomach renders taut the triangular peritoneal and fibrous support running from the diaphragm to the esophagus and upper part of the stomach; dividing this structure after clamping and tying, since it contains blood vessels, exposes the esophagus. Continued downward traction on the stomach causes the vagus nerves to stand out like whip cords and renders identification easy. Segments are removed from both nerves for microscopic verification.

8. *Removal of Gastric Segment.*—The completely mobilized stomach is now brought up into the wound, and two parallel 2¾ inch (7 cm.) Kocher clamps (fig. 3) are applied from the greater curvature side at right angles (fig. 4 *A*) to the long axis of the stomach at a point proximal

to the distal branch of the left gastroepiploic artery. The portion of stomach between the clamps is cut across to a point just beyond their tips, and a pair of 3½ inch (9 cm.) Kocher clamps are applied at right angles

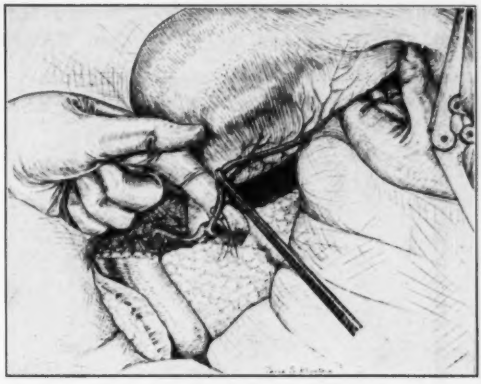

Fig. 2.—Ligation of the left gastric artery. The stomach is turned over to the left. The vessel is clamped, cut and ligated near its origin from the celiac axis. The vagus nerves are sectioned after this step.

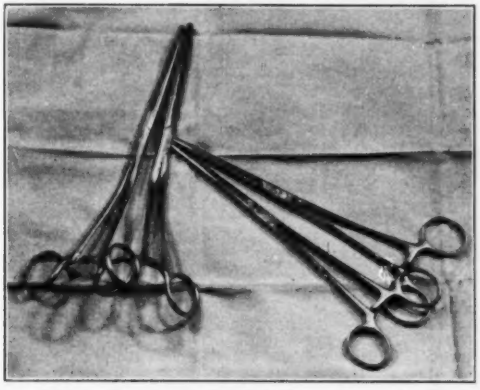

Fig. 3.—Modified Kocher clamps; 2¾ inch clamps used on the side of the greater curvature and 3½ inch clamps used on the side of the lesser curvature. The handles of the latter are curved to increase ease of application.

to the first pair in such a fashion that their distal extremities grasp the lesser curvature just at its junction with the esophagus. Resection is completed by cutting between the clamps (fig. 4 *B*). Inspection of

the removed area reveals that the entire lesser curvature, fully two thirds of the greater curvature and the continuous portion of the body of the stomach have been removed (fig. 5 *A*). This, in effect, achieves what is accomplished by the use of the Schoemaker clamp. We believe that removal of all the lesser curvature is of utmost importance (fig. 4). The upper clamp is now removed, and this portion of the stomach is

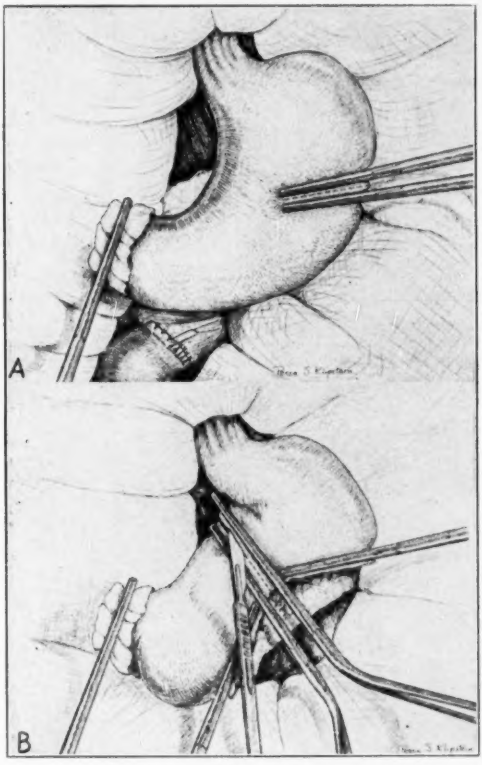

Fig. 4.—*A*, Kocher clamps applied at right angles to the long axis of the stomach at a point proximal to the distal branch of the left gastroepiploic artery. *B*, second pair of Kocher clamps applied at right angles to the first pair in such a fashion that all the lesser curvature will be removed.

closed by a double row of sutures (fig. 5 *B*). It will now be seen that a narrow elongated tube of stomach remains.

9. *Decision as to Type of Restoration of Continuity.*—A trial approximation of the gastric tube to the duodenum is now made (fig. 5 *B*).

If it is obvious that anastomosis can be made without tension, the von Haberer-Finney restoration is proceeded with; otherwise, a retrocolic gastrojejunostomy is carried out. Again we wish to emphasize that the decision regarding the type of anastomosis is not made until this stage of the operation is reached. Usually some additional mobilization of

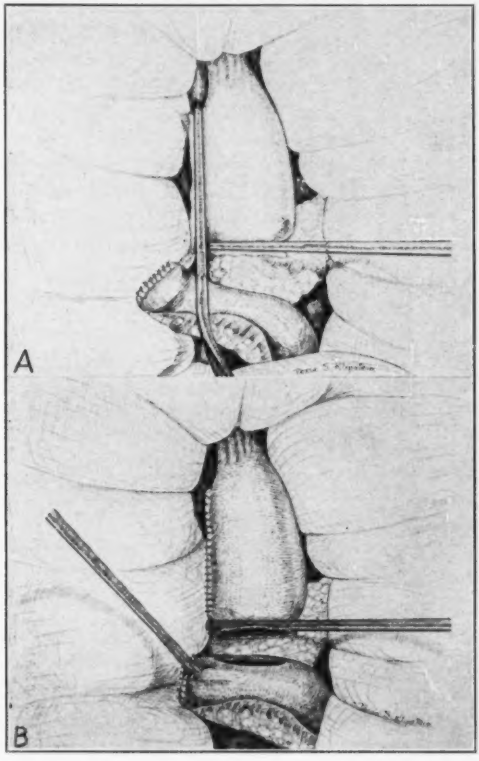

Fig. 5.—*A*, stump of stomach remaining. *B*, upper clamp removed and this portion of the stomach closed with a double row of sutures. Trial approximation of the gastric tube to the duodenum.

the duodenum and head of the pancreas must be done by further sectioning of the fascia propria. Rarely the hepatic flexure has to be mobilized downward by cutting its outer leaf of peritoneum, but frequently the right margin of the upper leaf of the mesocolon must be brushed downward to expose more of the descending duodenum.

10. *The Anastomosis.*—The posterior wall of the end of the stomach is sutured with interrupted fine silk sutures to the anterior wall of the duodenum close to the mesenteric border of the latter (fig. 6*A*). A suitable opening is now made in the duodenum, and the anastomosis is completed by a circular interlocking suture of atraumatic surgical gut

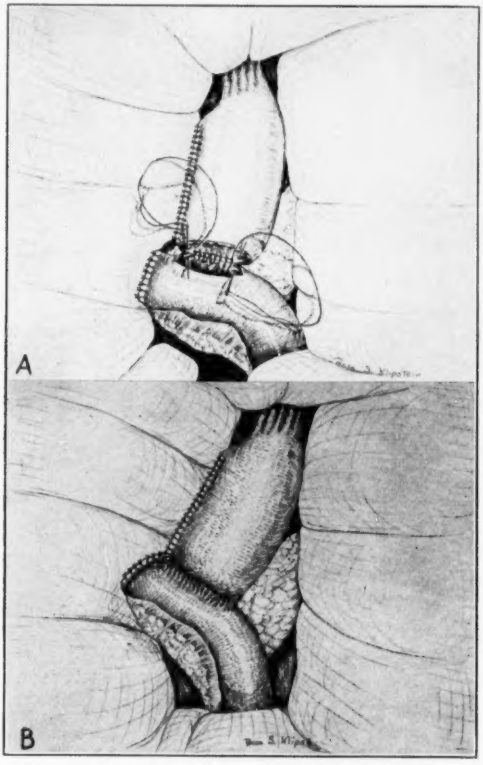

Fig. 6.—*A*, posterior portion of the anastomosis being completed. *B*, completed anastomosis. A purse string suture reenforces the upper angle of the anastomosis.

reenforced anteriorly with interrupted sutures of fine silk (fig. 6*B*). A precautionary purse string suture draws together the two gastric walls and the duodenum at the dangerous upper three way "angle of sorrows." The anastomosis, which readily admits two fingers, is freely mobile and lies without tension.

COMMENT

The important features of the operation on which success depends are:

1. Adequate mobilization of the duodenum and the head of the pancreas. This can be effected only by incising the fascia propria or endoabdominal fascia [6b] as well as the peritoneum along the outer border of the duodenum.

2. Tubing of the remaining part of the stomach. High section of the left gastric artery and the gastropancreatic omentum in which it lies produces maximum mobility of the stomach, as pointed out by the late W. J. Mayo.[2] Removal of the entire lesser curvature is a most important step in surgical treatment of peptic ulcer, as emphasized by Schoemaker, Aschoff and the late Roscoe Graham.[7] When these two important steps are completed and the new lesser curvature is reformed, it will be found that the narrow elongated gastric tube which remains can be approximated to the mobilized duodenum without tension.

3. Sectioning of the vagus nerves. This provides an additional 2 inches (5 cm.) in length to the stomach.

4. Making the anastomosis only when maximum mobility has been attained. The slightest degree of tension must be construed as being an absolute contraindication to gastroduodenostomy.

SUMMARY AND CONCLUSIONS

1. The von Haberer-Finney modification of the Billroth I gastrectomy extends the scope of this sound anatomic and physiologc method of restoring gastrointestinal continuity.

2. Success of the operation depends on adequate mobilization of the duodenum and stomach.

3. Application of the Schoemaker principle of tubing the stomach allows the surgeon to remove as much of the stomach as if restoration were completed by gastrojejunostomy.

4. Although insufficient time has elapsed to allow final conclusions to be drawn, the results so far suggest that the Billroth I principle has much to commend it.

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7. Graham, R. R.: Technical Surgical Procedures for Gastric and Duodenal Ulcer, Surg., Gynec. & Obst. **66**:269-287, 1938.

PRECAUTIONS AND RESULTS IN GASTRECTOMY

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IT IS WELL known that the operative mortality rate following gastrectomy has dropped to one third or one half of the figure encountered fifteen to twenty years ago.[1] The technic of performing gastrectomy and the ability of the surgeon have changed very little indeed during this period. It is obvious, therefore, that a better understanding of the physiology of the gastrointestinal tract with special consideration of preoperative and postoperative care is the major factor responsible for the improvement in the immediate results of gastrectomy. In preparation of this report we have studied material representing 191 gastrectomies for benign and for malignant disease in the Illinois Research Hospital during the past thirteen years. As is usually the case in other reports, our studies on postoperative complications and causes of death have made certain precautions quite obvious, which if utilized might have resulted in a greatly reduced number of complications and deaths. Many of the precautions listed subsequently have been used by us for years; others have only recently been adopted.

PRECAUTIONS IN PREOPERATIVE CARE

1. For any sick patient a complete examination to determine the presence or absence of complicating diseases is, of course, essential, along with carefully taken history. In patients with gastric lesions, many of whom have obstruction, certain laboratory examinations in addition to routine blood and urine examinations, including determinations of plasma proteins, nonprotein nitrogen and plasma chlorides, are essential in a patient's work-up. It is necessary to accomplish an accurate assay of the patient's physical reserve if operation is contemplated. It is

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1. Bell, H. G.: Problem of Gastric Cancer in a University Hospital, Surgery **23**:351, 1948. Walters, W.; Gray, H. K., and Priestley, J. T.: Carcinoma of the Stomach, Philadelphia, W. B. Saunders Company, 1942. St. Johns, F. B.; Harvey, H. D.; Ferrer, J. M., and Sengstaker, R. W.: Results Following Subtotal Gastrectomy for Duodenal and Gastric Ulcer, Ann. Surg. **128**:1, 1948.

remarkable how accurate an interpretation of the patient's ability to climb stairs and walk certain distances will be in estimating operability.

2. An accurate determination of the degree of obstruction must be made. If there is a history of vomiting or a history of sharp curtailment in caloric intake, obstruction is probably present. It is amazing how commonly a complete obstruction is encountered with only occasional or no vomiting. The most effective method of determining the amount of obstruction is to insert a tube into the stomach through the nasal cavity eight or nine hours after a meal. If the patient has eaten recently and obstruction is fairly complete, an ordinary Levin tube will often become plugged with food particles; accordingly, it is frequently wise to use a large stomach tube for the first examination. Any amount of fluid over 100 cc. represents obstruction. If several hundred cubic centimeters is found, it is usually advisable to maintain decompression with a Levin tube through the nares for two or three days. Frequently, after decompression and consequent relief of edema, the patient will be able to take a fairly large qauntity of food by mouth, at least for a few days, thereby improving his malnourished state.

3. Dehydration and hypochloremia must be corrected. If the patient has been taking very little or no fluid by mouth and has been vomiting, both of these conditions will be present. As much as 5,000 cc. of fluid may be necessary during the first twenty-four hours after admission if the patient has obstruction. No more than 10 Gm. of salt should be given per day, even in this early period, until the laboratory values for plasma chloride have been noted. It is not difficult to determine the amount of fluid needed after ten to twelve hours' observation, since the urinary output can then be measured and an estimate made from the amount voided. The urinary output in twenty-four hours should, of course, be 1,000 cc. or better.

4. Anemia must be corrected early. Several transfusions may be needed and should be given in the first two to three days of treatment to bring the patient's hemoglobin level hematocrit value and erythrocyte count to normal.

5. Hypoproteinemia must be corrected. Frequently, administration of enough blood to bring the hematocrit and hemoglobin levels to normal will likewise elevate the blood proteins to a normal or near normal figure. However, if hypoproteinemia exists in spite of adequate blood transfusions, active treatment is indicated, with a high protein diet and plasma and amino acids by the intravenous route; these will be the chief factors in reestablishing body protein.[2] In our hos-

2. (*a*) Lyons, C., and Myerson, H. S.: Hemoglobin Deficiency in Protein Depletion, J. A. M. A. **135**:9 (Sept. 6) 1947. (*b*) Clark, J. H.; Lyons, C., and others: Concept of Chronic Shock, Ann. Surg. **125**:638, 1947. (*c*) Varco, R. L.: Nutritional Preparation for Substandard Risk Patients, Surg., Gynec. & Obst. **84**:611, 1947.

pital, which takes care only of charity patients, the percentage of patients with at least some degree of obstruction accompanying their gastric lesions was as high as 30 to 40 per cent. Practically all of them manifest a hypoproteinemia along with a loss of weight varying from 10 to 30 pounds (4.5 to 13.5 Kg.) within the previous few months. Correction of this malnutrition is entirely essential before an operation can be considered.[2a,b] By obtaining an early estimate as to the amount of obstruction, we can obtain maximum caloric intake by giving the patient a liquid and soft diet containing 500 to 1,500 calories, supplementing it with plasma and amino acids intravenously. If the patient is able to take as much as 500 calories by mouth in twenty-four hours, his condition can invariably be improved by meticulous preoperative care over a period of several days. However, if the patient has sufficient obstruction to prevent any oral intake, it will be very difficult to improve his nutrition by intravenous therapy although dehydration and hypochloremia can obviously be corrected. The condition of the patient, including weight, etc., will be the factor determining how long the patient should be treated preoperatively with intravenous therapy (in the absence of oral intake) before resort to operation. If we do not have evidence of improvement in the patient's condition in three to four days, we submit the patient to operation at this time if obstruction at the pylorus is complete. Obviously a true subtotal gastrectomy in such circumstances will be associated with a high mortality rate.

6. Vitamin therapy is important when the patient shows evidence of malnutrition with decrease in oral intake from day to day. If the patient is able to take small quantities of food by mouth, the vitamins may be given orally; otherwise they will have to be given intravenously. In view of the severe deficit associated with semistarvation, more than the daily requirements will have to be given. For example, daily dosage equal to 20 mg. of thiamine hydrochloride, 5 to 10 mg. of riboflavin, 200 mg. of nicotinic acid and 200 to 400 mg. of ascorbic acid is indicated.

IMPORTANT POINTS IN OPERATIVE TECHNIC

Although the type of operation will be determined to some extent by the nature of the lesion, whether benign or malignant, high resection is indicated in either case, even though the lesion may be located in the pylorus. We prefer the posterior Polya operation but utilize an anteriar Polya and a Hofmeister Polya operation on certain occasions.

Regardless of the type of operation performed, Wangensteen [3] has shown that a relatively short afferent loop of jejunum should be

3. Wangensteen, O. H.: Importance of Short Afferent Duodenojejunal Loop in Gastric Resection for Ulcer, Bull. Minnesota M. Foundation **4**:82, 1944.

left between the ligament of Treitz and the lesser curvature of the stomach. However, we have not been particularly alarmed about an extra inch or two (2.5 or 5 cm.) of jejunum because we have not seen any marginal ulcers in the patients on whom we have performed an anterior Balfour-Polya operation, which of necessity leaves a longer afferent loop than does a posterior Polya operation. The only 2 marginal ulcers which we encountered in our patients on whom gastrectomy had been done at our hospital occurred in patients who had had a posterior Polya operation.

When a posterior operation is performed, it is essential that the edges of the mesocolon be anchored to the stump of stomach to prevent herniation with consequent intestinal obstruction. When the resection has been unusually high, great care must be exercised lest a kink be produced where the afferent loop joins the lesser curvature of the stomach. Since an obstruction at this point would be very dangerous from the standpoint of "blow-out" of the duodenal stump, it is commonly desirable in high resections to do a Hofmeister type of operation, turning in the medial half of the stomach and leaving the opening in the outer half adjacent to the greater curvature for anastomosis to the jejunum.

We have become convinced during our experience of the past few years that a duodenal ulcer should not be resected if its removal would leave such a short stump as to jeopardize its inversion. We have left 37 duodenal ulcers *in situ* and have had no complications arising therefrom. The only exceptions to this attitude in therapy, which is held by most surgeons, is in patients with active hemorrhage.

Not infrequently it will be very difficult or impossible to have a satisfactory inversion of the stump of the duodenum because of induration of the walls secondary to the ulcer and consequent inflammation. Occasionally sufficient duodenum may be freed from the inflammation involving the pancreas by inserting the index finger of the left hand into the duodenum while the dissection is being made. In instances in which even this is impractical, we resort to a procedure practiced by many in which we leave about 2 cm. of pylorus attached to the duodenum but are careful to excise all the mucous membrane.[4] This portion of the pylorus usually allows a sufficient turn-in, but if it is still difficult to obtain good inversion of the stump the two walls of the pylorus can be approximated with two rows of interrupted fine silk placed from the inside, but superficially to preserve all the blood supply possible. When this procedure is done, it is safer to add a third reenforcing layer by closing the end of the stump with a continuous

4. Schilling, J. A., and Pearse, H. E.: Re-Evaluation of Role of Pyloric Antrum in Marginal Peptic Ulcers, Surg., Gynec. & Obst. **87**:225, 1948.

0000 chromic surgical gut suture and cover the stump with omentum. Such a closure may be life saving in certain cases when induration of the duodenum makes inversion impossible or extremely dangerous. However, we wish to emphasize that closure by approximation is not as safe as inversion, although we have not had a duodenal leak with any stumps closed by the approximation technic.

Before the last few sutures in the anastomosis are taken we reach in with long forceps and thread the end of the Abbott-Rawson tube down through the efferent loop of jejunum. This allows us to feed the patient immediately and yet decompress the stomach.

It is not within the scope of this paper to discuss in detail the indications for vagus section. However, we can summarize our use of this operation by stating that we use it in all patients with marginal ulcers and in many elderly patients who are poor risks, particularly if obstruction is present. When it is performed, a gastroenterostomy should also be done, regardless as to whether or not obstruction is present, because vagus section is so commonly followed by pyloric spasm for a variable length of time. It is agreed by all that vagus section is not effective in gastric ulcer. Likewise, most surgeons agree that vagus section is very effective in the treatment of a marginal ulcer.

PRECAUTIONS IN POSTOPERATIVE CARE

1. Ample amounts of fluid are given to maintain urinary output of 1,000 cc. per day; it is true, however, that what appears to be adequate fluid intake for the twenty-four hour period immediately following operation rarely results in an output of 1,000 cc. There is an obvious oliguria for several hours following operation. In general, the amount of fluid per day should be equal to 2,500 cc. plus the amount obtained by decompression. We utilize 5 per cent dextrose and amino acids to a great extent.

2. The salt intake must be limited sharply during the immediate forty-eight hour period following operation.[5] We give no salt during this time except that which is contained in the amino acid solution. After the first forty-eight hour period little or no salt will be needed by vein, since in ordinary circumstances we are feeding the patient a liquid diet through the Abbott-Rawson tube; accordingly, he should be getting enough salt in his food unless he is draining unusually large quantities from the stomach.

3. The patient must be turned frequently and encouraged to cough as soon as he comes out of the anesthesia. We ambulate these patients the day following operation and daily thereafter except those who are

5. Coller, F. A.; Campbell, K. N.; Vaughn, H. H.; Iob, L. V., and Mayer, C. A.: Postoperative Salt Intolerance, Ann. Surg. **119**:533, 1943.

extremely weak because of malnutrition or other cause. If signs of atelectasis develop or if secretions are rather profuse, the patient will usually not be able to cough out the material himself. In such circumstances it will be necessary to insert a catheter through the nose and guide it into the trachea after the pharynx is sprayed with cocaine.[6] If this type of aspiration does not clear the mucus from the bronchi and if there is still residual evidence of atelectasis, there should be no hesitation in performing bronchoscopy with direct aspiration of the main bronchial stumps.[6]

4. To encourage deep breathing and minimize atelectasis, inhalations of carbon dioxide should be given every hour for the first few days except while the patient is asleep.

5. The Abbott-Rawson tube is removed on the third to the fifth day but only after it has been shown that the stoma is open. A fairly accurate estimation as to the function of the stoma can be determined by clamping the tube overnight and applying suction the next morning to determine how much fluid is retained in the stomach. This test is probably of more value if the patient is given 200 to 300 cc. of water to drink in the evening before the tube is clamped off. Although some patients are disturbed considerably by the presence of the Abbott-Rawson tube, the majority of them do not complain about it, and we therefore do not hesitate to leave it in place for five days, particularly since maintenance of daily caloric intake is important in most of our patients, who are so malnourished at the time of admission to the hospital.

ANALYSIS OF CASES

The material utilized as a basis for this report includes the cases of 191 patients in whom gastrectomy was performed at the Illinois Research Hospital during the thirteen year period from January 1936 to January 1949, inclusive.

These cases are presented according to diagnosis in table 1. Of the 191 operations performed, 114 were for benign and 77 were for malignant lesions. The gastric and duodenal ulcers were almost evenly divided, while in 11 cases both gastric and duodenal ulcers were demonstrated. There were 7 instances of marginal ulceration which had appeared after previous gastrectomy. Only 2 of these were in patients previously operated on at our hospital.

There were 75 gastrectomies for carcinoma. Forty-eight, or almost two thirds of these patients, had demonstrable metastases, and a few of these had purely palliative operations.

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6. Haight, C.: Intratracheal Suction in the Management of Postoperative Pulmonary Complications, Surgery **6**:445, 1939.

The types of operation utilized and the operative deaths associated with each are shown in table 2. There were 14 deaths in 184 subtotal resections, whereas in 7 total resections there was 1 death. The anastomosis was placed in a retrocolic position in 114 of the cases; in 60 it was found advisable to place the anastomosis anterior to the colon. In 7 instances resection of a gastroenterostomy stoma in addition to a subtotal gastrectomy was made necessary by the presence of marginal ulcers. In only 2 of these had the initial gastrectomy been performed in this hospital. Of the 7 marginal ulcers, 2 were further complicated by the presence of gastrojejunocolic fistulas. In these 2 cases the

TABLE 1.—*Summary of Partial and Complete Gastrectomies, Illinois Research Hospitals, January 1936 to January 1949*

Diagnosis		No. of Cases
Ulcer		114
Gastric	45	
Duodenal	51	
Gastric and duodenal	11	
Marginal	7	
Carcinoma		75
Regional metastases	48	
Lymphosarcoma		1
Reticulum cell sarcoma		1
Total		191

TABLE 2.—*Type of Operation*

		Number	Deaths
Subtotal gastrectomy		184*	14
Polya	174		
Resection of gastroenterostomy stoma	7	...	0
Hofmeister	3	...	0
Total gastrectomy		7	1
Total		191	15

* Resections of the cardia and terminal end of the esophagus are not included.

patients were similarly treated by resection of the stomach and the involved portion of the colon after preliminary colostomy.

The postoperative period was without complication in 123 cases in this series. There were a total of 88 complications which presented themselves in the remaining 68 patients. These complications and their incidence are presented in table 3. An analysis of these complications revealed that the deaths were centered for the most part in a relatively few of the complications. Therefore, we present in table 4 the complications which made specific contributions to the mortality herein reported.

Cardiac complications were responsible for 3, or 20 per cent, of these deaths and pulmonary complications in the form of atelectasis, pneu-

monia and pulmonary embolism contributed another 20 per cent of these deaths. This leaves 60 per cent of our mortality rate that resulted from complications which we consider preventible. Wound disruption occurred in 4 per cent of this series and was responsible for 1 death. There was 1 death from massive hemorrhage in a bleed-

TABLE 3.—*Complications Following 191 Gastrectomies*

		Number	Deaths
Atelectasis		19	1
Pneumonia		13	2
Wound infection		11	0
Wound disruption		9	..
Peritonitis		7	..
Obstruction		7	..
Stomal	5	..	0
Intestinal	2	..	1
Perforated duodenal stump		4	3
Peritoneal abscess		3	0
Diarrhea		3	0
Pulmonary abscess		3	..
Acute heart failure		3	3
Pulmonary embolus		2	1
Perforation of jejunum		2	2
Urosepsis		1	1
Massive hemorrhage		1	1
		88	15

TABLE 4.—*Mortality Rate for Gastrectomies*

		Cases, Number	Mortality, Percentage
Subtotal gastrectomy		184	7.6
Carcinoma and sarcoma		70	11.4
Ulcer		114	5.2
Gastric	45 (6.6)*		
Duodenal	51 (5.8)		
Gastric and duodenal	11		
Marginal	7		
Total gastrectomy			
Carcinoma		7	14.2

* Figures in parentheses represent percentages.

ing duodenal ulcer. There were 2 deaths from jejunal perforations. One was the result of a jejunal ulcer adjacent to the anastomosis; the other was a perforation of a small hemorrhagic spot on the jejunum just distal to an esophagojejunostomy. It will be noted that postoperatively obstruction occurred in 7 cases; in 5 of these the site of obstruction was the stoma. There were 2 instances of obstruction of

the efferent jejunal limb. One of these was a result of simple kinking and was relieved by operation; the other was a result of torsion of the jejunal loop which encouraged the efferent limb to migrate posteriorly and to the right of the afferent limb. The result was gangrene and death. The most dangerous complication encountered was leakage of the duodenal stump, which occurred in 4 cases. In 1 of these the cause of death was determined at necropsy to have been atelectasis, the leaking stump being only an incidental finding. The deaths of the other 3 patients were charged directly to the leak in the duodenal stump.

The mortality figures are presented in table 4. In 184 subtotal gastrectomies there were 14 deaths, constituting a mortality rate of 7.6 per cent. Eight of the patients who died had carcinoma or sarcoma, giving a mortality rate for malignant lesions of 11.4 per cent. The remaining 6 deaths were of patients operated on for complications of ulcers, with a resultant mortality rate of 5.2 per cent for benign lesions. There were 3 deaths each of patients operated on for duodenal and for gastric ulcers, with the mortality rates for the two groups of lesions being slightly higher in the latter group. There was 1 death among 7 patients subjected to total gastrectomy, or a mortality rate of 14.2 per cent.

COMMENT

The steadily improving mortality rate associated with gastrectomy has been quite generally observed. Credit for this encouraging trend doubtless lies in many factors, including improvements in methods of anesthesiology, the advent of the antibiotics and chemotherapeutic agents, increasing familiarity of surgeons with the procedure and, as previously mentioned, a better understanding of the physiology of the gastrointestinal tract. We feel that the emphasis on physiology as it is related specifically to the preparation and postoperative care of these patients is the most important single factor in the progressive improvement in results from this operation.

The patient who presents himself with a gastric or duodenal lesion today, even without obvious obstruction, is recognized to be nutritionally depleted until proved otherwise. With the laboratory reports properly evaluated in the light of the usual study of loss of weight, we deny or confirm the existence of that state of nutritional depletion which Lyons and Mayerson [2a] have termed "chronic shock." These workers, as have Varco [2b] and others, emphasized the importance as well as the methods of correcting these nutritional deficiencies prior to operation. The recognition that these poor risk patients, once their nutritional equilibrium has been restored, may become fair or even good risks has contributed to the broadening scope of the indications for gastrectomy.

We were particularly interested in the complications contributing to mortality as presented in table 5.

The cardiac and pulmonary complications together represented 40 per cent of the mortality reported. The deaths from cardiac complications occurred in patients whose cardiac status had been evaluated by medical consultants who assisted in their preparation for operation. We are inclined to classify them as unavoidable. The pulmonary complications were responsible for 3 or 20 per cent of the deaths, but it is to be noted that the incidence of these pulmonary complications, including atelectasis, pneumonia and pulmonary embolus, totals 34, or 55 per cent, of these potentially fatal complications. We therefore feel that we have kept fatalities from pulmonary complications near the minimum. There remains for consideration 60 per cent of the operative mortality here reported. Eight of these 9 deaths we feel may be classed as avoidable.

TABLE 5.—*Complications Contributing to Mortality*

	Incidence	Deaths
Atelectasis	19	1
Pneumonia	13	1
Wound disruption	9	1
Obstruction	7	1
Duodenal stump leak	4	3
Acute heart failure	3	3
Pulmonary embolus	2	1
Perforation of jejunum	2	2
Massive hemorrhage	1	1
Urosepsis	1	1
Total		15

The leaking duodenal stump has been recognized as the complication most to be feared in gastrectomy. In general, its incidence is greater in gastrectomy for duodenal ulcer than in gastrectomy for gastric ulcer, because the presence of the ulcer in the duodenum will interfere with inversion of the duodenal stump. This relatively greater incidence of leakage of the stump following gastrectomy for duodenal ulcer usually results in a higher mortality rate than in gastrectomy for gastric ulcer. However, in our series, the mortality was approximately the same in the two groups, perhaps because we have been exceedingly careful in closure of the stump when the gastrectomy was performed for duodenal ulcer.

The death from massive hemorrhage occurred in a duodenal ulcer previous to the formation of our present policy, which calls for surgical intervention in bleeding ulcers which fail to maintain circulatory stability once it has been established or in those who present a history of more than two severe incidents of bleeding.

There were 2 jejunal perforations, 1 of which was in a marginal ulcer. The more generous resections routinely accomplished today

tend to decrease the incidence of the gastrojejunal ulcers and consequently, of the complications that may arise therefrom. The other jejunal perforation was through a small hemorrhagic spot near an esophagojejunal anastomosis, most likely the result of inadvertent trauma.

The 7 patients with postoperative obstruction included 5 in whom the site of obstruction was the stoma. Of these, 4 were relieved by conservative measures and 1 required reoperation. None died. There were 2 patients with obstruction of the efferent jejunal limb. One of these had simple kinking which was relieved by operation. In the other the obstruction was the result of torsion of the jejunal loop with resultant gangrene and death. The latter 2 cases emphasize the point made by Mayo[7] of the importance of the proper placement of the efferent jejunal loop so that it descends from the gastrojejunostomy into the left abdominal fossa posterior to the remaining part of the small bowel.

SUMMARY

Progress made in the knowledge of physiology during the past twenty-five years resulting in improved preoperative and postoperative care has unquestionably been a much more important factor in lowering mortality rate during this period than has improvement in surgical technic. Important precautions in minimizing the mortality rate following gastrectomy are correction of dehydration, electrolytic imbalance, anemia and hypoproteinemia before operation is performed. In our estimation the use of the Abbott-Rawson tube has been of definite value in postoperative care in our patients. Likewise, in our estimation, limitation of the salt intake to no more than 1 or 2 Gm. during the first two days postoperatively has been an important factor in eliminating postoperative oliguria.

This study includes a survey of 191 gastrectomies performed at Illinois Research Hospital during the past thirteen years. The mortality rate was 11.4 per cent for subtotal gastrectomy for carcinoma and 5.2 per cent for ulcer, or an average of 7.6 per cent for the series of 184 subtotal gastrectomies. During the past few years the mortality has obviously been lower than during the first part of the period studied. It is anticipated and expected that the rate in gastrectomy for benign ulcer at the present time should be less than 3 per cent.

Atelectasis was the commonest complication but accounted for only 1 death. Pneumonia was diagnosed in 12 cases, but only 1 of these patients died. The highest number of deaths from any single complication occurred in leakage of the duodenal stump (13 deaths) and cardiac disease (3 deaths).

7. Mayo, W. J.: Technic of Gastrojejunostomy, Ann. Surg. **43**:539, 1906.

DISCUSSION OF PRECEDING PAPERS

DR. JAMES T. PRIESTLEY, Rochester, Minn.: The very careful studies of Drs. LaBree and Gillespie are illuminating. I think that one of the points which Dr. LaBree made is worth while emphasizing—namely, the importance of the amount of stomach resected in the treatment of duodenal ulcer. It is very difficult to evaluate results of partial gastrectomy for duodenal ulcer which are reported in the literature if the amount of the stomach resected is unknown. Obviously, the physiologic basis for the operation is the reduction of gastric acidity, and the results will vary depending on the amount of the stomach removed. The type of anastomosis performed would seem to be of secondary importance.

I do not know that it has ever been shown that it makes a tremendous difference how much of the stomach is resected so far as the "dumping syndrome" is concerned. Possibly it does make a difference, but it has been my impression that in this particular regard the type of anastomosis is a factor of importance.

Regarding Dr. Fallis' paper, I certainly agree that the Billroth no. 1 operation has many features which appeal from the physiologic point of view. With this operation normal anatomic relationships are more closely preserved, which always seems desirable, and, secondly, it is a simpler procedure technically than an anastomosis of the remaining portion of the stomach to the jejunum. On the other hand, it should be emphasized, as Dr. Fallis mentioned, that this operation should not be decided on until an adequate amount of the stomach has been removed and should not be performed if there is any tension at all on the suture line, as in those circumstances difficulties may follow.

I wondered why Dr. Fallis seemed to prefer the von Haberer type of Billroth no. 1 operation, as it seems to me that this requires more in the way of duodenal mobilization and suture lines than the Shoemaker type, which was illustrated in his figure 5, in which the lower end of the stomach is anastomosed directly to the end of the duodenum.

Regarding Dr. Eastman's paper, I should like to ask him a question concerning postoperative complications in the small group of cases in which the exclusion type of resection was performed after removal of mucosa in the remaining pyloric antrum. It has been my feeling in doing this type of operation, although I do not do it often, that I never can be quite satisfied with the closure of the stump, and in circumstances in which resection, severing the gastrointestinal tract through the duodenum, is not feasible, I have thought that it might be better to do some other type of operation rather than to take a chance with the stump.

As emphasized by Dr. Eastman, I think that we have been remiss in the past in providing an adequate caloric intake for the patient during the first week or so after gastric resection. Even though tube feeding is employed, total caloric intake during this period may be less than one would desire unless a careful check is made of the actual nutritive value of the food supplied. On the other hand, many patients after gastric resection do not require an indwelling tube. They are able to take food by mouth very early during the postoperative period, and the surgeon should be certain in these circumstances that sufficient calories are provided to meet the metabolic needs of the patient. Several years ago my colleagues and I discovered that the diet which we employed after operations on the stomach did not fulfil the daily needs of the patient until almost a week after operation, which obviously is undesirable. There is, of course, no

doubt that adequate nutrition is a factor of great importance during any postoperative convalescence.

Dr. Warren H. Cole, Chicago: In the discussion of gastrectomy, I should like to emphasize the great value of the Abbott-Rawson tube, since it allows one to start feeding the patient even the same day as the operation and yet maintain continuous decompression of the stomach. Nutrition is particularly important in our patients, since all are of the charity type and many are malnourished when first seen.

Regarding perforations of the duodenal stump after gastrectomy, we have had too many of those. They are usually commonest in gastrectomy for duodenal ulcer, because the ulcer complicates inversion of the stump, but in our series the incidence was just as high in gastrectomy for carcinoma.

Our experience, though small, might suggest that obstruction caused by a kink of the proximal arm of jejunum at its point of anastomosis to the lesser curvature is probably a greater cause of "blow-out" than anything else. Accordingly, one should always inspect this area at the termination of the operation but preferably should try to estimate before starting the anastomosis whether or not kinking may occur.

In general, an obstruction at this point would be most likely to occur in extremely high resections, and in such cases the Hofmeister procedure will shorten the proximal loop of jejunum and thus minimize the danger of obstruction.

Dr. Eastman remarked that we had 2 marginal ulcers in our series of gastrectomies. Both occurred in the posterior Polya operation. We had none in our anterior Polya operations.

I think that brings up an important point because some people have been talking about the necessity of having a very short proximal loop of jejunum and about the danger of doing the anterior operation. Since we did not have any in our anterior Polya resections, I am not so inclined to worry about the danger of doing anastomoses anterior to the colon if I think there is indication.

Not long ago it was considered necessary to excise the ulcer when doing a resection of an ulcer. However, of late years most surgeons leave the ulcer in place if it appears that resection would be dangerous. By leaving the ulcer when its resection might be difficult or would jeopardize closure of the stump, I am sure that we are lowering our mortality rate and not increasing the difficulties postoperatively. At any rate, we have no postoperative symptoms or other difficulties which might have been explained by failure to remove the ulcer.

We have had 3 or 4 cases which might be classified as instances of the dumping syndrome, but they were very inconsistent, and I am not sure that we had more than 1 true case of dumping syndrome. None of these occurred in the Hofmeister operation.

I wish to emphasize that the mortality rate of gastrectomy has decreased even during the past five years. Our over-all mortality rate for benign lesions during the twelve year period was a little over 5 per cent. However, of recent years it is less.

I feel sure that at the present time almost all important surgical groups are operating on benign lesions with a mortality rate of under 3 per cent. The mortality rate in gastrectomy for carcinoma will be twice that for benign lesions.

Dr. Henry K. Ransom, Ann Arbor, Mich.: In general, my experience with gastrectomy has been similar to that which was reported by the essayists. In the past, the duodenal exclusion operations of Devine and Finsterer have been employed

for certain duodenal ulcers in which resection by the conventional method would have entailed difficulty in obtaining a satisfactory closure of the duodenal stump. The results have been far from satisfactory.

Thus, in 14 cases of simple transection of the stomach through or above the antrum and reconstruction by an end to end gastrojejunostomy (Devine), follow-up studies showed that only 2 patients were well, 3 were improved and in 9 the results were poor.

In 22 patients treated by Finsterer's resection for exclusion, 7 were well, 5 were improved and 10 had poor results. When the Finsterer procedure was modified by exenteration of the mucosa of the antral segment in 29 cases the results were: well, 25; improved, 1, and poor, 3. For the present I have discontinued the use of vagotomy in order to evaluate more fully the results thus far obtained. An interim evaluation of 57 cases of gastroduodenal ulcer treated by vagotomy alone or in conjunction with some other procedure (excluding resection) shows the results to be good in 35, or 61.4 per cent; fair in 16, or 28.1 per cent, and poor in 6, or 10.5 per cent.

Dr. M. G. Gillespie, Duluth, Minn.: As co-author of the paper read by Dr. LaBree, I might just say that we have felt, so far as vagotomy or vagotomy and gastroenterostomy is concerned, that there are others in a better position than we to judge this procedure. Secondly, we have felt that not enough time has elapsed to judge properly the question of vagotomy or vagotomy and gastroenterostomy. The third reason that we continue and will continue to perform what we consider adequate partial gastrectomy is that, although we know that it is not an ideal operation, for the patient with chronic complicated duodenal ulcer it offers a gratifying result in a high percentage of cases.

Dr. Laurence S. Fallis, Detroit: In reply to Dr. Priestley's question as to why the von Haberer–Finney modification was used instead of the Billroth no. 1 operation, the point I wish to make is that one can extend the scope of the Billroth no. 1 technic by using this modification. In many cases of penetrating duodenal ulcers it is often difficult and sometimes impossible, at least for me, to make a satisfactory end to end anastomosis. I have, therefore, chosen this method because of its safety factor.

I agree with Dr. Cole that the most important item in duodenal blow-out is the prevention of back pressure, and it is just in this type of patient, in which one feels insecurity of closure of the duodenum, that the von Haberer–Finney lateral anastomosis will add the safety factor, since it eliminates back pressure on the duodenal stump.

It seems to me that one point in the technic of closing the duodenal stump that has not been emphasized enough is mobilization of this organ. I am accustomed to telling my residents that I have learned much of my surgery backward, that I had never learned how to take care of a difficult appendectomy until I resected a few right colons and, by the same line of reasoning, it was not until I had had the opportunity of mobilizing the head of the pancreas and the duodenum in the Whipple operation that I observed and recognized the value of this maneuver in resecting difficult duodenal ulcers. It is a much simpler matter to close the duodenal stump when the duodenum and head of the pancreas have been completely mobilized than when one has to do it in the depth of the wound.

Another item of importance in the security of closure is the importance of not separating the duodenum from the head of the pancreas to much. In other

words, some of the blow-outs are due to necrosis of the duodenal wall resulting from damage to blood vessels which inevitably follows undue mobilization of the duodenum from the head of the pancreas.

Dr. Ward H. Eastman, Chicago: In answer to Dr. Priestley's question, first, we prefer to turn in a duodenal stump whenever it is possible. When it is not possible, we prefer to turn in an antral stump, but we recognize a certain condition in which the thickness of the antral wall makes it dangerous to try to accomplish a turn of the antral stump, and it is in those instances that we turn to closure by approximation of the antral stump. We have 1 case in which a thick antral stump was turned in, and in retrospect we feel that if this case had been dealt with by approximation of the antrum we might have avoided this fatality. There have been no deaths in those instances in which we have found it advisable to close by approximation.

BLOOD TRANSFUSION AND REACTION IN SURGICAL PATIENTS

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PERHAPS there is no more important consideration when a transfusion of blood is requested than to remember the possibility of a complication during or after transfusion. For instance, the benefit to be gained from the transfused blood might not be important enough to the patient's progress to justify taking the chance of a possible untoward reaction. Nearly thirty years ago Pemberton [1] expressed the opinion that "the procedure is very often considered only a simple intravenous medication or a minor operation while in reality its potential dangers place it with major operations."

Possibly realistic views such as this one have been insufficiently appreciated, for it is known that even today a number of untoward reactions and occasional fatalities occur in a certain percentage of all instances in which blood is transfused.

In the last few years, and particularly during World War II, the thought, study and research expended on this subject exemplify the importance that is now being placed on the value of the transfusion of blood.

The inestimable benefits of, and the spectacular results obtained from, the administration of blood and plasma during the recent war constitute a subject apart from this paper. The great advances of the last ten years in knowledge about the use of this therapeutic procedure are by this time well known to almost everyone.

In fact, the average person today is more than mildly interested in the use of blood, plasma and other similar agents. The extensive work of the Red Cross in this field during the war did much to familiarize the public with the value of blood and how it is collected, stored and dispensed to the sick and injured. Many persons are superficially

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From the Section on Anesthesiology, Mayo Clinic.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 19, 1949.

1. Pemberton, J. deJ.: Practical Considerations of the Dangers Associated With Blood Transfusions, J. Iowa M. Soc. **10**:170-173 (June) 1920.

familiar with such things as blood groups, the Rh factor and the possibility of untoward reactions.

Because of the marked interest in the subject now manifested by members of the public and because we physicians owe everyone the best treatment that can be evolved, it behooves all physicians to be as familiar as possible with the indications for and contraindications to the transfusion of blood. Moreover, when this method of treatment is actually employed, the ever present possibility of the occurrence of an untoward reaction during or after transfusion must be constantly in mind. These untoward reactions have occurred and will continue to occur, even in the hands of the most skilled medical personnel and in the most meticulously supervised transfusion service. This fact must be accepted. However, to minimize the effects of these almost inevitable occasional reactions, we should be able to recognize the signs and symptoms which they produce, and we should know how to treat them.

Some physicians are under the impression that transfusion reactions will not occur if a patient is under the influence of an anesthetic agent. This idea we hope to dispel, because the truth is that all types of transfusion reactions do occur to patients during surgical procedures. Perhaps this wrong impression has arisen from the fact that transfusion reactions do occur among anesthetized patients, but the signs and symptoms frequently are masked by the action of the anesthesia, so that the reactions go unrecognized.

We shall not go into the details of such laboratory procedures as the determination of blood groups and Rh factors or the reading of cross matching tests that are important parts of a successful transfusion service. It may be said in passing that because of the absolute necessity of accuracy in the performance of laboratory procedures and the always present danger of human error, the laboratory plays a formidable role in a successful transfusion of blood. Every physician, of course, seeks to administer compatible blood, group for group, or low-titered group O blood to patients whose blood group is AB, A or B and to administer Rh-negative or Rh-positive blood as may be indicated.

Correct withdrawal and storage of blood from physically fit donors are essential. The administration of compatible blood is essential. Cross matching of donor's and recipient's blood is desirable. However, in dire emergencies it is our practice to administer blood without cross matching if time does not permit this procedure.

Even when all precautions have been taken to assure the administration of compatible blood, it must be expected that a certain number of untoward reactions will occur in both medical and surgical patients. Let us repeat what has already been said: that many reactions of minor character accompanying or following the transfusion of blood during surgical operations go unrecognized because the signs and symp-

toms engendered by the reactions have been masked by the effects of anesthesia.

When, however, an untoward reaction is manifested, it is very important to recognize it and to distinguish it from the underlying illness. During surgical operations this may be difficult, but if the physician is alert to the possibilities of such reactions they may, in most instances, be recognized. The seriousness of the situation varies according to the type of reaction which occurs. Therefore, we have felt that an attempt should be made to classify transfusion reactions so that a definite pattern of treatment for them can be set up.

At the Mayo Clinic it is the practice to divide all untoward reactions to transfusion into five categories: (1) pyrogenic, (2) allergic, (3) circulatory, (4) hemolytic and (5) a category known as "undetermined." In the last group are placed all bizarre reactions which may or may not be results of the administration of blood, but which, since blood was administered, cannot logically be omitted from possible consideration. It is possible, of course, that in maintaining such a category the transfusion of blood is sometimes wrongfully involved, but to ensure that no reaction will go unnoticed we must include those of which the cause is doubtful.

PYROGENIC REACTIONS

A pyrogenic reaction usually exhibits itself by a sudden chill and an increase in temperature of 1 to 4 degrees (F.); the increase in temperature appears either during or immediately after transfusion. The temperature usually will return to the level present before transfusion within four to eight hours unless something else supervenes. If this particular transfusion reaction occurs during or after an operation, the increase in temperature may be confused with the increase that ordinarily follows an operative procedure. When, however, the increase in temperature is the result of a transfusion reaction, it usually is greater than the average increase that follows the particular operation. Sometimes it may be difficult to distinguish, one from another, a very mild hemolytic reaction or a very severe chill and increase in temperature accompanying a pyrogenic reaction. The usual pyrogenic reaction does not produce free hemoglobin in the patient's serum and urine; this is one of the distinguishing differences between a hemolytic reaction and a pyrogenic reaction.

Depending on the indications for transfusion and on whether or not sufficient blood was transfused, a pyrogenic reaction usually does not interfere greatly with the desired therapeutic effect; for example, the expected increase in the quantity of hemoglobin and erythrocytes. When pyrogenic reactions are very mild, transfusion usually can be continued. When, however, they are severe, administration should be discontinued, at least temporarily.

Codeine or morphine as a sedative agent is valuable for a patient who is uncomfortable and has a chill. The external application of heat is appreciated by the patient; any further treatment is symptomatic.

ALLERGIC REACTIONS

An allergic reaction may occur not only in the conscious patient but also in a patient under the influence of general anesthesia. It may be very mild or extremely severe. Such reactions manifest themselves as urticaria or hives, and, if they are severe, as dyspnea, typical asthmatic rales and spasm of the smooth muscles. Still more severe reactions may resemble anaphylactic shock, which may be very quickly fatal. Fortunately, the milder forms of allergic reactions are the types most commonly seen.

Allergic reactions appear in about 1 to 3 per cent of transfusions. The exact mechanism is not known. We have observed allergic reactions in recipients of blood who never before exhibited allergic phenomena. We have also seen instances in which the same donor's blood, from the same bottle, administered to different recipients, had provoked allergic reactions in only one of the recipients, the others remaining free of any difficulty. Moreover, we have seen familial sensitivity, the recipient receiving blood from some member of his family on different occasions and becoming the victim of marked urticaria.

Occasionally, a donor has ingested a certain type of food a few hours previous to the donation of his blood. The recipient may be sensitive to that particular food and may exhibit allergic symptoms during or after transfusion.

The symptoms of an allergic reaction frequently are relieved by the subcutaneous or intravenous injection of 0.25 to 1 cc. of a 1:2,600 solution of epinephrine hydrochloride, provided that epinephrine is not contraindicated. One of the antihistaminic drugs administered to the patient during the allergic reaction is not quite so effective as it is when it is administered to the patient before transfusion was started.

If a recipient is known to be sensitive, certain precautionary measures can be taken: (1) A fasting donor can be obtained; (2) at the time of administration an adequate amount of an antihistaminic drug can be added to the bottle of donor's blood; (3) if it is deemed advisable, 0.50 to 1 cc. of a 1:2,600 solution of epinephrine hydrochloride can be added to the blood; (4) an antihistaminic drug can be administered to the patient orally or intravenously, and (5) additional treatment as found necessary can be carried out.

Occasionally, in spite of the foregoing precautions, the patient still exhibits allergic symptoms. In this event, a suspension of washed erythrocytes may be prepared. If these resuspended erythrocytes,

instead of whole citrated blood, are administered, frequently the allergic phenomena will not appear.

Despite the allergic reaction, the desired therapeutic effect usually is obtained from the transfusion.

CIRCULATORY REACTIONS

A circulatory reaction generally is encountered in patients suffering from some chronic cardiac disease. As a rule, the reaction is due to an overloading of the circulatory system, thus disturbing the cardiac or pulmonary mechanism. It is brought about by the administration of too great a volume of blood or the intravenous use of too large a quantity of fluids, too rapid an administration of blood or too rapid an intravenous infusion of fluids. Failure of the right side of the heart, accompanied with a decrease in blood pressure and a very rapid pulse, with sweating, pulmonary edema and cyanosis, appear. Fortunately, this complication is not seen frequently. Often when it is seen the prognosis must be guarded.

There should be no particular difficulty in making a diagnosis. Ordinarily this type of patient exhibits one of the contraindications to transfusion. If blood is to be transfused to such a patient, in spite of the contraindication, then extreme care should be exercised in administration of the blood. The first step in the treatment of circulatory reactions is prophylaxis.

When this complication does make its appearance, inhalations of oxygen under pressure are indicated. It may be necessary to withdraw from the patient an amount of blood at least equal to that administered. Spontaneous recovery may occur.

HEMOLYTIC REACTIONS

For more than two centuries the successful transfusion of blood has been hindered by the grave manifestations of agglutination and hemolysis, resulting from the mixing of incompatible blood. Today, hemolytic reactions still constitute one of the most serious complications with which physicians must contend.

The reaction may be the result of the administration of incompatible blood, the administration of group O blood of too high a titer to a recipient whose blood is in group AB, A or B, the administration of blood already hemolyzed or the presence of intragroup and Rh incompatibilities.

Diagnosis.—At times the reaction is so mild that it goes unrecognized. At other times it is severe enough to end fatally for the recipient. The clinical manifestations generally are characteristic. The reaction usually occurs early in transfusion or immediately after its

completion. The patient's first symptoms are generalized tingling, with a sense of great discomfort and anxiety; lumbar pain; a cold, clammy skin; a decrease in the blood pressure; a very thready pulse; dyspnea, and cyanosis. Air hunger may be marked. Nausea and vomiting may be prominent. If the shock accompanying the reaction is successfully treated, the next prominent symptom is jaundice.

If the reaction occurs on the operating table, with the patient under the influence of general anesthesia, it is much more difficult to recognize the untoward reaction. It has been interesting to us that on three separate occasions, and on each occasion a different surgeon operating, much the same remark has been passed: "What has happened to the patient? I can't stop the bleeding." In none of these instances did anyone know that a hemolytic reaction was occurring. This disturbance of the bleeding and clotting of the blood sometimes results from the transfusion of incompatible blood. It may be followed by the oozing of blood from the site of transfusion, from the gums or uterus or from an incision in the skin.

When this reaction occurs, a sample of blood withdrawn from the recipient early in the course of the reaction should show considerable free hemoglobin in the serum. The urine becomes dark because of the presence of free hemoglobin and a paucity of erythrocytes.

Such a reaction may be so mild that it will go unrecognized. Generally, however, this is not the case. After the initial insult, there is an interval of a few days in which the condition of the patient seems to be progressing favorably. He may eat and sleep well and be well oriented. This may be followed by a phase of restlessness and drowsiness, progressing into stupor, convulsions and coma. Renal failure and anuria are damming back the nitrogenous waste products. Generalized edema and purpura may appear. If diuresis begins, the prognosis is better, but continued anuria is disappointing.

The early chills and fever may be mistaken for a severe pyrogenic reaction. On the other hand, the uremic state may be so late in appearing that the original illness may be wrongly blamed for the condition of the patient. Occasionally, it is difficult to decide whether death is due to incompatible blood or acute cardiac failure.

Hemoglobin in Plasma: When a hemolytic reaction follows transfusion, a sample of the patient's blood should be withdrawn. Five cubic centimeters of blood is drawn into a tube containing 0.50 cc. of a mixture of equal parts of 6 per cent solution of ammonium oxalate and 4 per cent solution of potassium oxalate. The blood is centrifuged, and the overlying plasma is examined for free hemoglobin. This procedure must be done soon after the appearance of the symptoms, because free hemoglobin disappears very quickly from the circulation. If the sample is withdrawn too late and free hemoglobin is not found,

a false sense of security may be obtained. All free hemoglobin may have disappeared from the circulation within four to five hours. If blood that is too old or is outdated is administered, free hemoglobin may be present in the circulation for two to three hours, after which bilirubinemia occurs and fades away in twenty-four to forty-eight hours. These particular changes may exhibit no symptoms at all.

Hemoglobin in Urine: A sample of urine passed after the transfusion of incompatible blood is smoky red, because of the hemoglobin. Oehlecker [2] has stated that hemoglobinuria does not occur unless 60 to 80 cc. of blood is hemolyzed. The coincidental presence of blood in the urine (metrorrhagia, hematuria) should cause no confusion because in these conditions numerous erythrocytes will be found and anuria is not one of the complications.

Retesting of Blood of Donor and Patient: Retesting of the donor's and the patient's blood for grouping and Rh factor and cross matching should be done. A sample of blood from the particular bottle from which the blood was administered to the patient should be tested for the grouping and Rh factor; cross matching should be done again. The element of human error could have intervened to cause bottles or labels to become mixed, with the result that the wrong type of blood was administered to the patient.

If fresh blood cannot be obtained from the donor, it may be possible to identify a less than average level of the alpha or beta agglutinins in the recipient's serum. This low level of agglutinins may be followed in a few days by a higher than average level of alpha or beta agglutinins. In this event, it should be suspected that the patient has received some incompatible group A or B cells.

Pathologic Considerations.[3]—The exact mechanism responsible for the hemolytic reaction is not completely understood. Phagocytosis of some of the erythrocytes takes place, but most of the incompatible cells are destroyed by the specific agglutinins in the patient's serum. It is generally accepted that the renal symptoms may be caused by the deposition in the renal tubules of the hemoglobin released from the destroyed cells. When the concentration of free hemoglobin exceeds a certain level in the circulation, the free hemoglobin is passed through the kidneys. The acute damage is seen in the tubules mechanically blocked by hematuric acid crystals and casts, degeneration and destruction of the epithelial cells of the tubules and swelling and cellular infil-

2. Oehlecker, F.: Die Bluttranfusion, in Hirschfeld, H., and Hittmair, A.: Handbuch der allgemeinen Hämatologie, Berlin, Urban & Schwarzenberg, 1934, vol. 2, pt. 2, pp. 1513-1592.

3. Mathieson, D. R.: Personal communication to the authors. Bennett, W. A.: Personal communication to the authors.

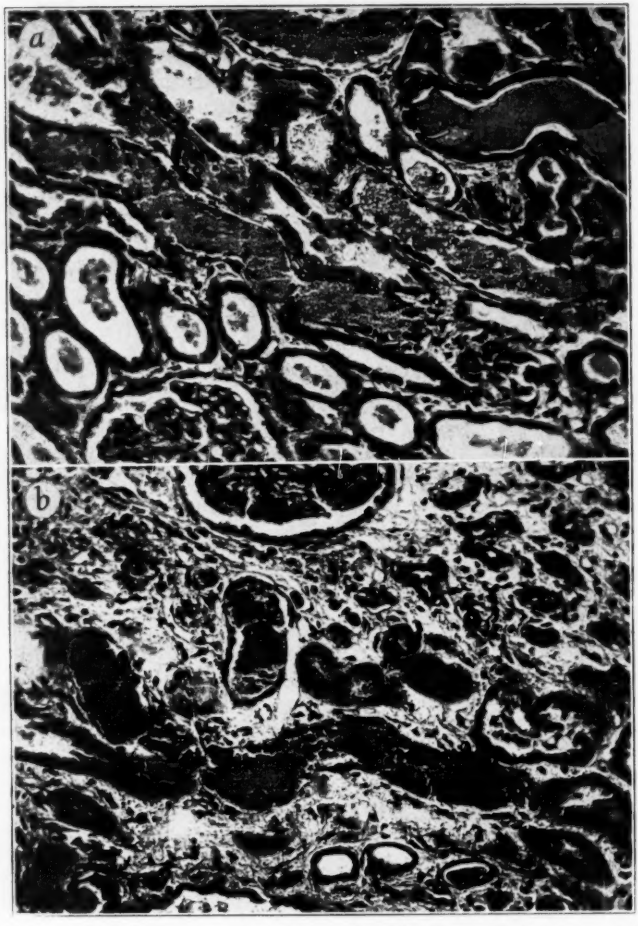

Fig. 1.—(*a*) Many casts are visible in the tubules: Several are granular in nature and one is a hyaline cast; the granular casts were stained with hemoglobin pigment; the tubule epithelium is undergoing degeneration, with a small accumulation of polymorphonuclear leukocytes, but the glomerulus tufts appear normal. (*b*) Necrosis of the epithelium, with casts present in the tubules: A few polymorphonuclear leukocytes are also seen about the casts and in the tubules; a few of these cells are also seen in the interstitial tissues. There is edema of the interstitial tissues. Hematoxylin and eosin; × 215.

tration of the kidney (figs. 1 and 2). Lucke[4] has presented a very fine explanation of this phenomenon.

The tubular obstruction in itself, however, is not adequate to produce renal insufficiency. Some other mechanism will be needed to explain the complete shutdown of renal function. Whether or not this is a vascular response to the hemoglobin by-products is open to question. This question has been thoroughly discussed by Trueta and his co-workers.[5]

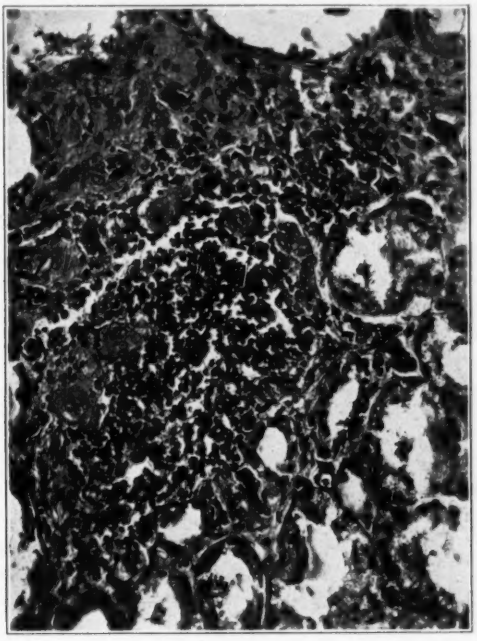

Fig. 2.—The accumulation of lymphocytes in the central area is accompanied with numerous giant cells. These giant cells contain old hemoglobin pigment. The tubules in the surrounding area are granular and swollen. This probably represents a granuloma which is in the process of picking up an old hemoglobin cast from a completely degenerated tubule. Hematoxylin and eosin; × 215.

4. Lucke, B.: Lower Nephron Nephrosis (Renal Lesions of Crush Syndrome, of Burns, Transfusions, and Other Conditions Affecting Lower Segments of Nephrons), Mil. Surgeon **99**:371-396 (Nov.) 1946.

5. Trueta, J.: Studies of the Renal Circulation, London, Oxford University Press, 1947.

Death occurring very soon after a severe transfusion reaction may reveal multiple thrombosis. When death occurs a few days later, the pathologic picture will be that already elaborated on.

Treatment.—In a case of suspected or proved hemolytic reaction, certain steps must be taken. In spite of the best treatment, death may follow such an untoward happening. On the other hand, the reaction may be so mild as to go unnoticed and without treatment. These steps are the following: First, if the offending blood is still running, transfusion should be stopped. Second, the patient must be supported in shock. The transfusion of known compatible blood, plasma or serum is in order. Third, the patient should be alkalinized with a 5 per cent solution of sodium bicarbonate or sixth molar sodium lactate solution. Fourth, the daily intake and output of fluids should be watched carefully. Two thousand to 3,000 cc. of fluid per twenty-four hours should be adequate. Care should be exercised that the patient does not receive too much sodium chloride. Aminophylline, human serum albumin or blood plasma may be administered to encourage diuresis. Fifth, if the patient becomes oliguric or anuric and the nitrogenous waste products are increasing, peritoneal lavage may be considered.[6]

UNDETERMINED REACTIONS

In the group of undetermined reactions, as has been said, are placed all bizarre reactions which cannot be definitely excluded as not being associated with or related to the transfusion. In such an event, the treatment must follow symptomatic lines.

CONCLUSIONS

The transfusion of blood is an important therapeutic method. In spite of the possibility of reactions and occasional fatalities, the proved value of the transfusion of blood far outweighs these disadvantages in most cases. Forty years ago Crile[7] made a very appropriate remark: "Judiciously employed, transfusion will surely prove a valuable, often life-saving resource; injudiciously used it will surely become discredited."

6. Odel, H. M.; Ferris, D. O., and Power, M. H.: Clinical Considerations of the Problem of Extrarenal Excretion: Peritoneal Lavage, M. Clin. North America **32**:989-1076 (July) 1948.

7. Crile, G. W.: Hemorrhage and Transfusion: An Experimental and Clinical Research, New York, D. Appleton & Company, 1909.

DIFFERENTIAL DIAGNOSIS OF JAUNDICE IN SURGICAL PRACTICE

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IN THE past two decades, several developments have influenced our clinical thinking in regard to jaundice. Many studies of the physiology of the liver in health have been made, and laboratory methods for studying hepatic disease have been developed. The latter have tended to detract from the time-honored and thoroughly tested clinical study of the jaundiced patient. The observations on the pandemic of infectious hepatitis during World War II have emphasized the importance of the parenchymatous type of jaundice. Some sequelae of this disease, such as homologous serum jaundice—serious and often fatal—acute and subacute atrophy and possibly chronic atrophy or cirrhosis, remain as current problems. Radical surgical procedures have been used for the relief of obstruction due to carcinoma of the ampulla of Vater and the head of the pancreas and for the relief of portal hypertension. Recognition of pancreatitis as a more frequent and clearcut syndrome has become disseminated and incorporated with other factors in our evaluation of jaundice. The discovery and clinical use of vitamin K have added immeasurably to successful therapy of jaundice, although some factors in regard to the hemorrhagic tendency of jaundice remain unexplained.

The surgeon is interested in the patient with jaundice for several reasons. One of the most important of these is that removal of an underlying lesion may produce a cure or some palliation. He knows that such a lesion is present in many cases of jaundice. He also knows that in certain instances operation can accomplish nothing and, in fact, may be detrimental to a high degree. He thus wishes to know whether the patient with jaundice should be treated by medical or surgical means. While he is chiefly interested in therapeutics and while he usually leaves the problem of diagnosis to his medical colleague, he should be sufficiently familiar with the causes and types of jaundice and with the necessary diagnostic procedures to enable him to give an intelligent opinion when he is called in consultation. This knowledge

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also will prevent him from knowingly or inadvertently performing an exploratory laparotomy in cases of parenchymatous jaundice and will insure that such an operation is performed in cases of obstructive jaundice.

The following statement by Moynihan has often been quoted: "No man is infallible in the diagnosis of jaundice." However, this is not a valid reason that an attempt toward infallibility should not always be made, especially since one has more tools to use in diagnosis than were available in Moynihan's day. Experience adds immeasurably to the facility with which the diagnostician arrives at his conclusions, but, no matter how great one's experience may be, medically or surgically, jaundice frequently continues to be misdiagnosed or mistreated. To lessen the number of cases in which this is true is the natural ambition of the members of the medical profession. Obviously, it is impossible to cover all details of diagnosis in this presentation; only the general principles can be outlined. Let it also be said at the outset that diagnosis should be established as early as possible in order that damage from delay in surgical treatment may be avoided and exploration of parenchymatous disease may be resisted. In the majority of instances, such diagnosis can be established reasonably, easily and early.

In approaching the problem presented by a patient with jaundice, one's orientation is influenced by certain precepts that training and experience have thoroughly ingrained in one's mental processes. Among these is a working classification of jaundice. Various classifications have been advanced, such as those of van den Bergh, McNee, Rich and Ducci. The most suitable for general clinical use would appear to be that of McNee, in which jaundice is classified as hemolytic, intrahepatic and obstructive. Although jaundice probably is never pure in type and although this classification is perhaps an oversimplification of the problem, it is a very practical one for therapeutic purposes, as it calls attention to the primary nature of the icterus.

Another precept is knowledge of the diagnostic points pertaining to the various syndromes. Hemolytic jaundice usually is readily recognized by the history, physical examination and appropriate examinations of the blood. Suffice it to say here that congenital hemolytic icterus, with its microcytic anemia, increased fragility of the erythrocytes and acholuria, is the principal example of hemolytic jaundice. It is important from the surgical standpoint because of the value of splenectomy in its management and the frequency with which gallstones are encountered in its course (60 per cent).

Intrahepatic or parenchymatous jaundice is characterized by involvement of the cells of the parenchyma and of the canaliculi. Various etiologic agents are responsible. The acute type is represented by epidemic and sporadic infectious hepatitis, homologous serum hepatitis and

toxic hepatitis, and the chronic type is represented by the various forms of cirrhosis, each with its characteristic syndrome. Pain seldom is an important feature, although at times it may be present and confusing in diagnosis. The bile ducts are patent, and rarely is there prolonged interference with the flow of bile. There usually is early and conclusive evidence of disturbance of the metabolic functions of the liver. Pruritus is not common. Intrahepatic jaundice, whether acute or chronic, is a medical problem.

Obstructive jaundice is commonly due to calculus, stricture or neoplasm and is a surgical problem. Serious disturbances of metabolic function of the liver usually are absent in the early stages. In cases in which a stone is present in the common bile duct, colic in association with the onset of jaundice is characteristic. The obstruction due to stone is seldom painless, seldom complete (perhaps in 10 per cent of cases), and the jaundice is usually mild and variable. Stone, nevertheless, may mimic any syndrome of intrahepatic or extrahepatic disease. Obstruction due to neoplasm is usually complete (90 per cent of cases), permanent and often painless. Stricture in the great majority of instances is readily recognized and follows soon after the performance of some surgical operation on the biliary tract, which is complicated by a stormy postoperative course and associated with either a deep persisting jaundice or the development of an external biliary fistula which intermittently closes and opens. Pain frequently is present, but true biliary colic is rare.

In considering the obstructive type of jaundice, the following facts should be recalled: (1) carcinoma of the gallbladder usually is associated with stones; (2) carcinoma of the head of the pancreas occasionally is associated with stones in the common bile duct or gallbladder; (3) recurrent strictures often are associated with stones above the site of obstruction, and the persisting obstruction and associated cholangitis of recurrent strictures not infrequently lead to the development of a secondary biliary cirrhosis; (4) in any case in which the obstruction persists for a month or more, secondary damage of the liver usually occurs, and (5) individual patients vary greatly in their tolerance to biliary obstruction. These facts often influence the ease or difficulty of diagnosis.

Another precept is a recognition of the relative frequency of the various types of jaundice. Published data vary considerably, depending on the type of practice they are collected from. Excluding hemolytic icterus, the majority of reports indicate that jaundice is of the intrahepatic type in from a third to a half of the cases and of the obstructive type in the remaining cases. In about half of the latter cases, the jaundice is due to benign lesions; in the remaining half, it is due to neoplasms. Obstructive lesions tend to occur in middle or later life,

and parenchymatous disease tends to occur in young persons. Gallstones are encountered more frequently in women than they are in men.

HISTORY AND PHYSICAL EXAMINATION

The history and the physical examination are and will remain the most important factors in the differential diagnosis of jaundice. The history is commonly developed around either the occurrence or the absence of pain. An accurate, detailed and chronologic account of the symptoms immediately or remotely preceding the onset of jaundice is most important and helpful. In cases in which the development of jaundice is associated with pain, the classic history is as follows: The patient has had chronic flatulent indigestion which has been punctuated by attacks of biliary colic which have necessitated the administration of opiates and often have been associated with chills, fever and sweats and have been followed by residual soreness and jaundice. This history is most characteristic of a stone in the common bile duct and in most instances is diagnostic. The jaundice may be mild, or even unnoticed in the early attacks. Darkening of the urine and lightening of the color of the stools may be all that the patient notices. Later, the jaundice becomes more obvious and persistent. Occasionally, it becomes deep and persistent owing to complete obstruction from impaction of the stone. While this classic history is the usual one in cases of stone in the common bile duct, the jaundice may begin painlessly (5 per cent of cases); colic may have occurred weeks or months prior to the onset of jaundice, and colic may be atypical in site and character (15 to 20 per cent of cases) or may develop after the onset of jaundice. While the colic is characteristic of a stone in the common bile duct it may occur in other conditions but is then more likely to be atypical in nature. These other conditions include carcinoma of the head of the pancreas, pancreatitis, cirrhosis and even the different types of hepatitis. At the onset of jaundice due to a malignant lesion, pain usually is absent in 40 per cent, mild in 35 per cent and severe or colicky in 25 per cent of the cases respectively. The severity of pain may be difficult to interpret. Some patients have a tendency to exaggerate; others have a tendency to minimize the severity of the pain. The latter is particularly true of the aged persons who have previously enjoyed good health and who may describe the pain of biliary colic as an attack of indigestion consisting of bloating and vomiting.

In cases in which an operation has been performed previously, it is important to inquire about the preoperative course of the illness, the surgical findings, the type of operation and the postoperative course. If a cholecystostomy only has been performed, usually for empyema of the gallbladder, persistence of jaundice obviously indicates an incomplete operation. If a cholecystectomy has been performed, persistence

of jaundice, the development or persistence of an external biliary fistula or the occurrence of colic, chills, fever and sweats and an increase in the jaundice usually mean an overlooked stone in the common bile duct, although these symptoms occasionally are due to an overlooked carcinoma of the head of the pancreas or of the ampulla of Vater or to pancreatitis. However, if jaundice had been absent before cholecystectomy was performed but develops during a stormy postoperative course and becomes deep and persistent or if the operation is followed by an external biliary fistula that closes intermittently in association with pain, fever and deepening of the jaundice, it usually may be assumed that the common bile duct has been injured.

In taking a history in a case in which jaundice has begun without abdominal pain, one should attempt to determine (1) whether or not the patient recently has been exposed to an epidemic of infectious hepatitis; (2) whether or not he recently has received any parenteral therapy, such as transfusion of whole blood or pooled plasma; (3) whether or not he recently has had an infection of the respiratory or gastrointestinal tract; (4) whether or not he recently has ingested any medicinal substance or has been exposed to any other toxic substance which might have caused injury of the liver, and (5) whether or not he recently has had a malignant tumor removed or has had any general symptoms which might indicate the development of an unsuspected malignant tumor.

In acute hepatitis, slight fever, malaise, anorexia, nausea and even vomiting may precede the onset of jaundice. In cirrhosis, the first symptom may be sudden hematemesis or the onset of ascites. In many cases of painless jaundice, there are no significant preceding symptoms. A history of premonitory or accompanying symptoms may not necessarily be diagnostic of the type of jaundice, but it may furnish circumstantial evidence or may even be misleading. For example, malignant disease may cause jaundice in the midst of an epidemic of hepatitis. Absence of historical data leaves the situation indeterminate, and the diagnosis will have to depend on physical data and laboratory procedures, with or without a period of observation.

The presence or absence of pruritus is not diagnostic. However, pruritus has a definite tendency to occur in cases of obstructive jaundice, especially if the biliary obstruction is high grade. It is often absent in the mild jaundice associated with a stone in the common bile duct, and it is occasionally absent in cases of complete biliary obstruction. In intrahepatic disease, it does not occur frequently, even if the disease is severe, and when it is present it is not often severe. It is often severe in cases of cirrhosis, especially primary biliary cirrhosis.

Physical examination may permit a definite diagnosis to be made, or it may be of little value in the diagnosis of jaundice. Special atten-

tion should be given to the size and consistency of the liver and spleen, to the presence of a palpable gallbladder, to evidence of carcinoma elsewhere and to the presence of vascular spiders. Hepatomegaly is not often diagnostic; however, marked enlargement of the liver is most suggestive of carcinoma. If the surface of the liver presents definite hard nodules, a malignant lesion almost certainly is present. A palpable distended gallbladder in the absence of inflammation nearly always means neoplastic obstruction of the common bile duct below the junction of the cystic duct and can be demonstrated clinically in 60 per cent of cases in which there is such an obstruction. When demonstrable, it is one of the most diagnostic of all physical findings. Chronic inflammatory disease of the gallbladder or previous cholecystectomy or obstruction above the junction of the cystic duct and common bile duct obviously prevents this finding. The gallbladder may be distended but not palpable if the abdominal wall is obese, muscular or unrelaxed or if an overhanging edge of the liver interferes with adequate examination. An enlarged, hard, nodular gallbladder suggests a malignant lesion of this organ.

Other physical findings worthy of note are (1) tumors elsewhere in the body, particularly in the region of the pancreas, supraclavicular lymph nodes and rectal shelf; (2) spider angiomas, which have been said to be the trademark of cirrhosis; (3) collateral venous circulation in the abdominal wall and esophagus; (4) abdominal scars and fistulas; (5) factitial dermatitis; (6) melanosis of the skin; (7) xanthomas; (8) edema; (9) ascites; (10) pallor, and (11) ecchymosis or other evidence of bleeding. Mention also should be made of the tint of the jaundice. The golden yellow or orange color of the skin most frequently seen in hepatocellular disease is often in marked contrast to the green hue of obstructive jaundice. This difference in color is not invariable and is not accepted as diagnostic in all quarters, but when present it furnishes a clue to the pathologic condition that is present.

PATENCY OF THE BILE DUCTS

After the history and physical examination, establishment of patency or occlusion of the bile ducts is the next important step in the diagnosis of jaundice. In some cases, this may already be evident, and no further diagnostic procedure may be indicated. However, in cases of deep painless jaundice, further investigation is necessary. Visual examination of the stools is of little aid if the jaundice is deep. The stools may appear acholic whether or not the jaundice is due to obstruction or intrahepatic disease. Chemical examination of the feces for urobilin is equally unreliable. There are, however, two fairly satisfactory procedures which are useful in establishing patency or obstruction of the bile ducts. These are duodenal intubation and quantitative determina-

tion of the urobilinogen in the feces. When duodenal intubation is performed, the position of the tube should be checked by roentgenologic examination if no bile is obtained. Recovery of bile means that the liver is secreting bile and that the bile ducts are at least partially patent. Failure to obtain bile indicates either complete obstruction of the bile ducts or complete suppression of the secretion of bile at the time of intubation. The latter rarely persists long, if it actually occurs, and bile is usually obtained if the intubation is repeated a few times. If bile is persistently absent, complete and permanent obstruction is usually present. Duodenal intubation may serve a further useful purpose. The recovery of gross blood is suggestive of an ampullary lesion or of a carcinoma of the pancreas which is ulcerating into the duodenum.

Determination of the urobilinogen content of the feces should be carried out with great care. Collection of the feces for at least seventy-two hours is necessary. The determination should be repeated from time to time during the period of observation to determine whether permanent obstruction of a bile duct or temporary suppression of bile is present.

In cases in which jaundice is caused by a malignant lesion of the extrahepatic biliary tract, the bile ducts usually are completely and permanently occluded, whereas in cases of parenchymatous jaundice they are patent. Duodenal intubation and quantitative determination of the urobilinogen in the feces are used to determine this obvious and fundamental difference between the two types of jaundice. Exceptions to these findings occur under the following conditions: 1. In an occasional case of malignant disease, the obstruction may be incomplete and suggest the presence of parenchymatous jaundice. 2. In an occasional case of malignant disease, complete obstruction may become incomplete and the jaundice may tend to disappear; as a result, the presence of parenchymatous jaundice may be suspected. 3. In an occasional case of severe parenchymatous jaundice, especially in the first ten to fifteen days, there may be nearly complete suppression of the secretion of bile and the presence of complete obstruction may be suspected.

ROENTGENOLOGIC EXAMINATION

Roentgenologic examination seldom furnishes conclusive diagnostic data in cases of jaundice. Cholecystography has little to offer in cases of jaundice, and the results of this procedure may be misleading. Occasionally, it reveals a primary shadow of the gallbladder, which indicates disease of this organ. In some instances, roentgenograms of the upper part of the abdomen may demonstrate biliary or pancreatic calculi. However, in the presence of deep, painless jaundice, the demonstration of a stone or stones in the gallbladder should not be interpreted as

necessarily indicating the presence of a stone in the common bile duct. The possibility that the jaundice may be due to a malignant lesion or to primary parenchymatous disease of the liver should not be ignored. Indeed, either of these is more likely than a stone in the common bile duct. Roentgenologic examination of the esophagus, stomach and intestine is valuable in demonstrating the presence or absence of esophageal varices and intrinsic malignant lesions. Occasionally, widening of the duodenal loop may indicate enlargement of the head of the pancreas. Choledochograms are useful in studying biliary fistulas or patency of the bile ducts if a drainage tube is situated therein.

CHEMICAL EXAMINATION AND TESTS FOR HEPATIC FUNCTION

The first, and probably the most important, chemical examination which should be performed in any case of jaundice is the measurement of the amount of bilirubin in the serum. This is done best by use of the van den Bergh reagent, although the determination of the icterus index may be utilized. Several satisfactory procedures for the former are available. The presence of direct-reacting bilirubin in the serum does not differentiate hepatogenous from obstructive jaundice. Furthermore, the amount of direct-reacting bilirubin cannot be commonly used for this purpose, because it is increased in both intrahepatic and obstructive jaundice. The quantitative determination of serum bilirubin, however, furnishes some information that is of definite value in determining (1) the degree of icterus; (2) the course of the jaundice, if repeated determinations are carried out, and (3) the cause of the icterus. If the concentration of serum bilirubin is 12 to 20 mg. per hundred cubic centimeters, it indicates either complete obstruction or severe hepatogenous icterus; if it is higher than 25 mg. per hundred cubic centimeters, it indicates severe parenchymatous disease, which is usually primary but may be secondary to obstruction. Concentrations which are less than 10 mg. per hundred cubic centimeters usually mean that any obstruction present is not complete.

The remaining chemical tests are usually described as liver function tests. They have been developed partly to aid in distinguishing obstructive jaundice from parenchymatous jaundice but chiefly for studying disturbances of the metabolic functions of the liver. Their multiplicity and the constant addition of new tests indicate that no single test or combination of tests is entirely satisfactory. Some of these tests have been utilized by Watson as part of his "profile" study of jaundice. The table shows the results of some of these tests in cases of obstructive jaundice and in cases of parenchymatous jaundice. Their use is based on the fact that in cases of obstructive jaundice a disturbance of metabolic function seldom occurs unless the jaundice has been present

for a long time or is complicated by infection, whereas in cases of parenchymatous jaundice a definite disturbance of metabolic function usually becomes evident early in the course of the disease. They are not intended as a substitute for clinical study and judgment, but they may extend the range of accuracy of diagnosis. Some of them are generally accepted as a necessary and important part of the study of cases of jaundice.

The value for plasma cholesterol is increased in about 80 per cent of cases of obstructive jaundice, while it is normal or decreased in about 90 per cent of cases of primary parenchymatous jaundice. However, major exceptions may be encountered, such as an increased value in cases of parenchymatous jaundice and a normal or low value in cases of obstructive jaundice. Normally, more than 50 per cent of the plasma cholesterol is combined with fatty acids. Low values for cholesterol esters are most frequently obtained in cases of primary disease of the

Results of Tests of Hepatic Function in Cases of Obstructive Jaundice and Parenchymatous Jaundice

Test	Results	
	In Obstructive Jaundice	In Parenchymatous Jaundice
Concentration of plasma cholesterol	Increased	Normal or decreased
Concentration of serum alkaline phosphatase	Increased	Normal
Cephalin-cholesterol flocculation	Negative	Positive
Thymol turbidity	Negative	Positive
Effect of vitamin K on prothrombin time	Prompt	Delayed or absent

liver, the degree of lowering being roughly indicative of the degree of parenchymatous damage.

Earlier investigators of the value of serum alkaline phosphatase claimed that values above 10 units (Bodansky) strongly supported the presence of an obstructive type of jaundice and values below 10 units indicated the presence of a hepatogenous type of jaundice. Later investigators became skeptical of the diagnostic value of the concentration of the serum alkaline phosphatase because of the many exceptions. Nevertheless, alterations in the value for the serum alkaline phosphatase, taken in connection with other findings, may be of considerable help in differential diagnosis.

The cephalin-cholesterol flocculation test of Hanger and the thymol turbidity test of Maclagen are dependent on alterations in the serum proteins and lipids. Definitely positive reactions in the presence of deep jaundice usually mean active destruction of the hepatic parenchyma. Because of this, positive results with these tests usually are obtained early in acute and subacute hepatitis and late in obstructive jaundice. However, exceptions occur; negative results, for some

unknown reason, are at times obtained in parenchymatous disease and positive results may be encountered in obstructive jaundice. The results must be correlated with other data. Nevertheless, in cases of deep jaundice, when operation is being considered, a positive thymol turbidity test should not be ignored. It should necessitate a careful review of all other data.

The prothrombin time should be determined in every case of jaundice and in every case of disease of the liver. If it is increased, a prompt return to normal on administration of vitamin K is indicative of obstructive jaundice, whereas its failure to return to normal or a slow return to normal indicates failure of utilization of vitamin K, which is the result of serious hepatic injury.

In general, the pattern revealed by these tests in cases of obstructive jaundice is characterized by an increase in the concentration of both plasma cholesterol and serum alkaline phosphatase, a negative cephalin-cholesterol flocculation reaction, a negative thymol turbidity reaction and a prompt response of the hypoprothrombinemia to vitamin K. In cases of parenchymatous jaundice, the pattern is characterized by a decrease in the concentration of both cholesterol and cholesterol esters in the plasma, a concentration of serum alkaline phosphatase of less than 10 units (Bodansky), a positive cephalin-cholesterol flocculation reaction and a positive thymol turbidity reaction. The response of hypoprothrombinemia to the administration of vitamin K usually is delayed, although it may be absent or occasionally prompt. In cases of chronic disease of the liver, the concentration of serum albumin is decreased and that of the serum globulin is increased. In an appreciable percentage, perhaps 20 per cent, of cases of parenchymatous disease of the liver, the results of these tests are normal or resemble those obtained in cases of obstructive jaundice. This has been explained on the basis that the hepatic lesion involves the cholangioles rather than the polygonal cells. On the other hand, in some cases of obstructive jaundice the results of these tests resemble those usually obtained in cases of parenchymatous jaundice. In such cases, the obstruction usually has been present for a long time or a parenchymal change has occurred as a result of the obstruction.

COMMENT

A careful study of the clinical history, the physical findings and the results of tests for patency of the bile ducts and for hepatic function will result in a positive diagnosis in 80 to 90 per cent of cases of jaundice. In the remaining small percentage of cases, there may be reasonable doubt in regard to diagnosis. The history may be confusing, the physical findings meager and laboratory data equivocal. In the individual case, theory and the clinical and laboratory findings may

not coincide. Evidence may be conflicting. The most troublesome cases are those in which the onset of jaundice is painless. In such cases, parenchymatous jaundice may be confused with malignant obstruction, especially if the obstruction is incomplete. Some physicians would consider all such cases of painless jaundice as cases of parenchymatous disease until proved otherwise, particularly in view of the recent pandemic of infectious hepatitis. In the majority of cases of parenchymatous jaundice, the icterus will disappear in two to eight weeks. In cases of obstruction, the jaundice will persist.

In cases of parenchymatous jaundice, exploratory laparotomy may lead to serious results. On the other hand all are aware of the occasional case of painless jaundice in which relief is obtained by the removal of gallstones which have been silent and overlooked. In such cases, however, no harm will result from keeping the patients under careful observation for a reasonable time, at least until it is determined that acute or subacute hepatitis is not the basic disorder. Few surgeons have not had the experience of inadvertently performing a laparotomy in a case in which medical treatment was indicated, and few internists cannot count among their cases some in which the patients have been denied a curative operation. Such errors are usually due to a hurriedly taken or incomplete history, to overlooking something on physical examination, to inadequate laboratory investigation, to misinterpretation of data or to insufficient observation. It may be necessary to check and recheck the history, never forgetting that useful information may be obtained from the family or the family physician. A repeated physical examination may reveal some new findings that may clinch the diagnosis. Judicious repetition of some laboratory tests from time to time may be illuminating. One always should keep in mind the relationship of the time factor in cases in which some of the tests for hepatic function subsequently furnish useful information. Experience assists clinical judgment and may permit some short cuts in diagnosis, but, in general, it is not wise to pursue these too far. It is like the master of a ship directing his vessel without carefully charting his course and observing all possible bearings.

In conclusion, it is desirable to state some of the surgical indications and contraindications in conditions associated with jaundice. The former include (1) a reliable history of gallstones or colic or both; (2) proved intermittent biliary obstruction, usually due to a stone in the common bile duct but occasionally due to stricture or to both stricture and a stone and indicated by fluctuating jaundice, colic, fever and chills; (3) proved complete and permanent biliary obstruction, usually indicative of a malignant lesion; (4) an external biliary fistula, either intermittent or persistent, usually indicating a stone in, or a stricture of,

the common bile duct or both a stone and a stricture, and (5) painless jaundice appearing within six months after cholecystectomy and usually due to traumatic stricture, provided serum hepatitis is not present.

These indications may be considered conservative, and the surgeon may properly decide to proceed with operative intervention on much less definite ground. Whether the indications are clear or not, the following relative contraindications should always be given consideration in making the decision. These are directed at the avoidance of surgical procedures in cases in which jaundice is caused by injury to the parenchyma of the liver alone and include (1) recent exposure to hepatotoxic agents and infectious hepatitis and transfusion of plasma or whole blood within two to four months; (2) signs of serious hepatic disease, such as vascular spiders, visible collateral circulation, edema and pronounced hypoproteinemia; (3) intense jaundice (serum bilirubin in excess of 25 mg. per hundred cubic centimeters with patent biliary passages; (4) decidedly chronic jaundice with splenomegaly, a condition formerly described as primary biliary cirrhosis and more recently as cholangiolitic cirrhosis; (5) hypoprothrombinemia that is refractory to vitamin K, and (6) a positive result of a thymol turbidity test.

SUMMARY

When a detailed chronologic history has been taken, a careful physical examination made and patency or occlusion of the external biliary tract established in a case of jaundice, it is possible in the majority of instances to classify with considerable confidence the jaundice into one of the three fundamental groups: hemolytic, intrahepatic and obstructive. It also is possible to clarify the surgical indications or contraindications and to determine whether the jaundice due to obstruction is the result of a stone, a stricture or a malignant lesion. Laboratory investigation may lend material assistance in confirming the clinical diagnosis, may be actually diagnostic or may warn of danger in performance of an exploratory operation and indicate a delay. In a small group of cases, the diagnosis may remain uncertain and a period of further observation with a careful review of all data and judicious repetition of some of the laboratory procedures may be in order. Even then in a few instances an exploratory laparotomy may be necessary before the diagnosis can be established with certainty. Mistakes of both commission and omission are usually the result of failure to secure all obtainable data, of attempted short cuts and of misinterpretation of data. If strict adherance to established tenets and procedures is maintained, the differential diagnosis of jaundice can be approached with confidence and success and the surgical indications can be thoroughly clarified.

DISCUSSION OF PRECEDING PAPERS

DR. FORRESTER RAINE, Milwaukee: In reference to Dr. Seldon's discussion of hemolytic reactions, I think one might consider an additional form of treatment that he did not mention. I had occasion recently to be interested in a patient who received 500 cc. of incompatible blood, when my associate who is in charge of the transfusion service was called in to take care of her. She did not get a very violent clinical reaction, but in twelve hours it was noted that her urine was absolutely black and her blood at this time was black also. She had had an output of only 200 cc. of urine at the end of twelve or fourteen hours after her operation.

An exsanguination transfusion was done, removing and giving her 12 pints (5.7 liters) of blood. At the close of that time her blood, which had been black at the start, was of a rather good red color and her urine began to increase in amount almost at once and was pretty clear immediately afterward; by the next day it was entirely normal. The patient made an uneventful convalescence.

It seems to me that one can assume that renal damage does not necessarily occur all at once in these instances but is progressive, and possibly, if enough of this agglutinated hemolyzed blood can be removed, we may prevent sufficient damage to the kidney to produce anuria, which did not develop in this patient.

DR. WALTER G. MADDOCK, Chicago: I should like to ask Dr. Ravdin to say a few words on his experience with the intravenous use of hydrolysate solutions and their possible benefit in relation to this work on hepatic damage.

DR. I. S. RAVDIN, Philadelphia: The question of the nutritional state of the patient is one that we have been interested in for some time, and we have belatedly come to the conclusion that the best way to feed a patient is by mouth. There is no known method now of intravenous therapy which will satisfy all the nutritional requirements of the patient over a period of time. One can, if the oral method is not available, save the patient considerably by intravenous therapy, but there is no indication that would permit one to draw any conclusion other than that such therapy is extravagant and wasteful when the oral method is available. Nitrogen balance studies mean little unless one knows that the nitrogen has been used in the protein pool of the body. For instance, one can give gelatin intravenously and produce a positive nitrogen balance, but one well knows that large amounts of the gelatin are stored in the body as gelatin and naturally therefore the patient may actually be in negative nitrogen balance. The same is true of the use of human serum albumin which is not readily used in the protein pool of the body. The evidence which Dr. Liegel and her group in our laboratories obtained is exactly similar to the evidence reported by Dr. Madden, that one can obtain positive nitrogen balance with a smaller amount of nitrogen by mouth and with somewhat less calories than one can if one attempts to produce a similar circumstance by intravenous feeding in man. There can be no doubt but that when one is attempting to produce regeneration of the liver in man, one must take into account not only the composition of the diet but also the fact that over a period of days in the preoperative period the patient must ingest a large number of calories—3,500 to 5,000 calories a day. This cannot be obtained by any other means than providing the patient with the dietary which the patient will eat. We are convinced that if such a dietary is provided by mouth—and usually patients will eat it—it had best be a complete dietary of whole components of foodstuffs, rather than predigested protein.

There is some reason to believe that if the liver on the verge of incompetency has thrown into it large amounts of predigested components that liver may be thrown into incompetency. We are not entirely sure of the latter fact, but the

problem of distention and its effect on the liver was found during experiments designed to test that very problem.

DR. J. DEWEY BISGARD, Omaha: What if one had to depend on another route—if the oral route was not available or usable? What would be your routine in maintaining nutrition?

DR. I. S. RAVDIN, Philadelphia: We would use just exactly what every one of you uses then, the substances that are available, the protein hydrolysates and glucose. We have from time to time used various fat preparations that have been prepared for us. We have not as yet had a satisfactory stable preparation for the injection of fat by the intravenous route, but we should increase our total caloric intake if we had such a preparation readily available by the utilization of fat, and in these circumstances, if one introduces a sufficient amount of split protein which contains a sufficient amount of thiamine—and especially choline—one would not expect the amount of lipid in the liver to increase.

DR. T. H. SELDON, Rochester, Minn.: I was interested in the remarks of Dr. Raine. In the Institute of Experimental Medicine, Mayo Foundation, a Fellow is working on a project whereby it is hoped to be able to transfer the blood of 1 animal to a second animal by a continuous pump system. The second animal, it is hoped, will be able adequately to look after the needs of renal excretion for both animals. To date this work has not been completed. From a clinical point of view we have thought of the possibility of doing exsanguination transfusions on patients. I am interested to know that this has been carried out successfully in practice.

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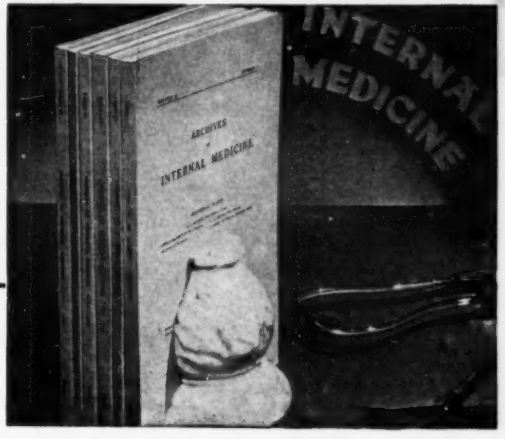

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